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JENNER'S COWPOX INOCULATION*

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The introduction of vaccination as a prophylactic measure against smallpox by Jenner in 1798 was for many years the only successful application of active immunization in the prevention of infectious disease. The development of Jenner's method and its application to other infections by Pasteur 80 years later marked the beginnings of the science of immunology as we know it to-day. Great advances have been made in the last 20 or 30 years in the field of virus infections; but Jenner's method of immunization against smallpox still stands as the most valuable specific prophylactic measure against diseases caused by these agents.

The practical value of vaccination at the present time is perhaps not so immediately apparent as in Jenner's day, and to put the discovery in its proper setting it is necessary to consider briefly the morbid influence of smallpox at that time. The disease had been endemic in England for several hundred years, and early in the eighteenth century was said to be the cause of 70 to 80 out of every 1,000 deaths. During the course of the century, in spite of, some people think because of, variolation, to which I will refer presently, the ravages of the disease in no way abated. Haygarth in 1793 stated that in previous years the ratio of deaths from smallpox to births was as 1 to 6¼ in London, 1 to 6½ in Manchester, and 1 to 5½ in Liverpool. Most of the population were destined to suffer from the disease, and Haygarth records that after the outbreak in Chester in 1774 only one-fourteenth of the population had not had smallpox. The mortality from smallpox was then around 15 to 20% of cases, and most of the deaths occurred in children under 10 years. In Chester, from 1772 to 1777 inclusive, of 1,105 deaths in children under 10, 369—that is, one in three—were due to smallpox (Haygarth, 1793).

Inoculating the Smallpox

Variolation, or the practice of communicating smallpox artificially, was of ancient origin, and had apparently been used in Pembrokeshire before it became generally known to the public in this country through the activities of Lady Mary Wortley Montagu in 1721. It was based on the experience that, when the infection was transmitted by applying smallpox matter through scratches or incisions in the skin, the disease was likely to be much less severe than when contracted in the ordinary way. Variolation was used by lay people in Turkey and Greece as well as in Wales and the Highlands of Scotland, but the medical profession were not practitioners of this measure. Lady Montagu had had her son inoculated with smallpox in 1717 by Mr. Maitland, surgeon to the embassy in Constantinople, where her husband was British Ambassador. In 1721, after the family had returned to London, she had her 4-year-old daughter variolated, again by Maitland. This event created some stir in medical and society circles in London; but, even after further trials on convicted felons and orphanage children and the variolation of two children of the royal family without untoward effect in 1722, the practice did not become popular.

It early became apparent that the method was not without risk. In October, 1721, Maitland inoculated Mary Batt, aged 2 years, daughter of a Quaker living near Hertford. The child had a mild attack of the disease, having only 20 pustules, and soon recovered. But six of the domestic servants contracted smallpox from the child and one of them died. Nor was the disease in the inoculated person always mild. The Earl of Sunderland's son, inoculated by Maitland in April, 1722, died of the infection. The introduction of variolation into Ireland in 1723 was particularly unfortunate, for of the first 25 inoculated in Dublin three died, two of these of haemorrhagic smallpox. In 1726 Maitland inoculated six children in his native Aberdeenshire, and one of these died; in this part of the country the practice was not again taken up for 20 years.

During the first eight years after its introduction only 897 were inoculated for smallpox in England, and of these 17 died. During the next 10 years inoculation was apparently little practised, but was again restored in England, apparently because of reports of its success in America. In 1746 public subscriptions were raised for the purchase of houses in London to be used as an inoculation hospital. This was not popular in the neighbourhood because of the fear of spread of the disease, and patients leaving after their stay of several weeks were abused and insulted in the streets, so that it became usual for them to leave in the hours of darkness. From 1751 variolation made uninterrupted progress, helped by a powerful sermon by the Bishop of Winchester in 1752 and by the approval of the College of Physicians, who considered the practice highly salutary to the human race. At this time the method of inoculation and care of the patients was such that the death rate from inoculated smallpox was less than 1 in 200.

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Improved Methods of Inoculation

The practice increased in popularity by the improvement in methods introduced by the Suttons, particularly by Daniel Sutton, who left his father to begin practice on his own in Essex and in Kent in 1763. Moore (1815) wrote of him: "Daniel Sutton with secret nostrums propagated inoculation more in half a dozen years than both faculties of medicine and surgery with the aid of the Church and example of the Court had been able to do in half a century." Dimsdale, himself probably the most successful medical practitioner of variolation, acknowledged his indebtedness to Daniel Sutton, whose methods he followed. Dimsdale (1781) attributed the success of Sutton to the method of inoculation by light scarification or puncture, the use of lymph from the primary vesicle of a previous patient or from an early vesicle in a casual case, the absence of dressing at the site of inoculation, the ambulant treatment followed, and the use of cold water to alleviate thirst at the febrile period. But while Sutton's innovations were to the benefit of his patients, the freedom of movement allowed them during the eruptive fever and afterwards tended to spread infection throughout the community.

As variolation was practised mostly among those of means, it was the poor who suffered from the increased prevalence of the disease. To minimize the risk of spread from inoculated persons Dimsdale and Haygarth recommended periodic inoculation of all those in a community who had not previously suffered from smallpox; those who were inoculated were enjoined, until they were recovered, to avoid contact with people who had not had the disease. Some of those variolated had no general eruption, but it was shown that the lesion at the site of inoculation might be the source of smallpox in immediate contacts; and the mildness of the disease in the inoculated did not necessarily ensure a similar benign course in those who acquired infection from them.

In spite of his success as an inoculator and the rarity of unfavourable results, Dimsdale later condemned the practice: "Though the loss under inoculation is very inconsiderable . . . yet by spreading the disease, a great proportion take it in the natural way; more lives are now lost in London than before inoculation commenced, and the community at large sustains a greater loss; the practice, therefore, is more detrimental than beneficial to society" (quoted from Monro, 1818). Even with the improved methods the fatality rate from inoculation towards the end of the eighteenth century was estimated at 1 in 250 to 1 in 500. Adams in 1807 wrote: "No patient is inoculated for smallpox without anxiety to the practitioner, the patient, and his friends"; and Woodville (1796) says of the early years of variolation: "That inoculation did not constantly succeed in producing the distinct or favourable kind of smallpox was at that time, and still continues to be, a melancholy truth."

Jenner's "Inquiry"

It is little wonder, therefore, that Jenner's method should have been so eagerly accepted as an alternative to variolation, although some of his medical brethren were unwilling to give up the older practice. For, as Jenner claimed, the cowpox inoculation was not infectious and did not carry with it the risk to the patient which variolation incurred. But let us consider for a moment the evidence on which Jenner's claim for cowpox inoculation or vaccination as a protection against smallpox was based. The first cases listed in Jenner's *Inquiry* comprised 20 persons who had been infected by contact with diseased cows from less than a year up to 50 years before they were unsuccessfully inoculated with smallpox matter. In 11 of these variolation was attempted in the years 1791 to 1797, and one had been unsuccessfully inoculated in 1778. Three persons had become infected from horses. One, inoculated with smallpox matter six years later, failed to develop the disease, one developed a mild smallpox after variolation, and the third had a mild smallpox infection following exposure to casual infection. In addition to these there was one boy who was inoculated with cowpox vesicle fluid from the hand of Case 16; six weeks, and again several months, after he had recovered from the ensuing illness he was inoculated with smallpox vesicle fluid without effect.

In 1798 another boy was inoculated with matter from a cow, and from the resulting vesicular lesion on his arm the infection was passed in series through four more children. At the third passage several children and adults were vaccinated, and at the fourth three children; the fifth transfer was made to a boy 7 years old. Of this series three, including the last boy, were later inoculated with smallpox virus without effect. In his subsequent discussion Jenner points out the great advantage that inoculation of the cowpox would have over variolation, as it involved no risk of spreading a disease that filled the country with terror. None the less, Jenner realized that his evidence did not prove the case for cowpox inoculation, for he finished the *Inquiry* with the following sentence: "In the meantime I shall myself continue to prosecute this inquiry, encouraged by the hope of its becoming essentially beneficial to mankind."

Support for Jenner

Evidence in support of Jenner's observations was soon forthcoming. Within a few months of the publication of the *Inquiry*, George Pearson, a physician to St. George's Hospital, published reports by others who likewise had failed to variolate persons who had recovered from casual cowpox. When a fresh supply of cowpox lymph became available early in 1799, many people were inoculated in London by Pearson and Woodville, and, as lymph was widely distributed in England and on the Continent from this source, vaccination rapidly spread in spite of a certain amount of opposition. As the practice of variolation also continued for some years in the nineteenth century there was ample opportunity for testing the vaccinated by subsequent inoculation of smallpox virus. This was in fact done, and in the subsequent publications of Jenner (1801), Pearson (1802), Willan (1806), and others there are reported several hundred instances of people who had been vaccinated and in whom subsequent variolation failed to produce disease. Forty years later Robert Ceely (1842) gives details of 21 persons who had been successfully inoculated with a fresh cowpox strain that he had introduced and who were tested 5–31 months later with smallpox matter. None of these developed smallpox, though in some there was produced what we would now call an accelerated reaction.

In two points in the *Inquiry* Jenner probably erred in his conclusions. He expressed the belief that matter from an affection of the heels of horses known as "the grease," transmitted by the hands of men who also milked cows, was the source of cowpox; and that only

after it had passed to the cow did it "invariably and completely possess those specific properties which induce in the human constitution symptoms similar to those of the variolous fever, and effect in it that peculiar change which for ever renders it unsusceptible of the variolous contagion."

Jenner admitted that he had not been able to prove by actual experiment that the source of infection of the cow was a peculiar morbid matter arising in the horse; this supposed origin received no support from the experiments of subsequent observers, who failed in many attempts to induce cowpox in cows by inoculation with material from grease in horses. (As Crookshank (1889) has related at length, however, it was later shown by Loy, in England, Sacco, in Italy, and various observers in France that from horsepox, a febrile disease with a generalized vesicular eruption, humans and cattle could be inoculated with results similar to those following cowpox infection. From the infection of horses, equine strains of virus were brought into use for inoculation against smallpox by Jenner and workers on the Continent.) Nor was it long before it was shown that persons successfully inoculated with cowpox virus might later suffer from smallpox, though usually in a mild way. Details of such cases were published by Willan (1806), Adams (1807), and later by Monro (1818) and Cribb (1825). Cribb notes that smallpox in the vaccinated had been more frequent of late years—an observation not surprising in the light of present knowledge concerning the waning of immunity with the passage of time.

Establishment of Vaccination

Vaccination, however, quickly became much more widely practised both in this country and abroad than variolation ever had been. Cribb records in 1825 that the percentage of the population who had been vaccinated varied in different parishes between 34 and 69—a rate not achieved in diphtheria immunization until many years after the introduction of the method in this country. Vaccination was, however, carried on from arm to arm, and it appeared that as a result of repeated passage in this way the virus became uncertain in its effects. Vesiculation did not always result from inoculation. New sources of lymph were therefore sought and fresh strains from affected cows, or from milkers directly infected from cows, were introduced by Estlin (1837–8), Ceely (1840), and others. Such new strains produced much more vigorous local reactions, which took longer to heal and were frequently accompanied by axillary adenitis and fever; although Estlin (1839) noted that after 48 removes from the cow his strain had lost much of the activity it possessed when only 15 removes from the cow. Ceely tried retrovaccination of the cow in an attempt to rejuvenate stock strains of "humanized" lymph; but in this country it was not until near the end of the nineteenth century that virus propagated in the skin of calves received official approval for the preparation of vaccine lymph. Ballard (1868) notes that in Italy and France lymph had been kept going in cattle from 1863 and 1866 respectively. He also states that it was impossible to trace the origin of lymphs then in current use in England.

The viruses now used for the preparation of vaccine lymph in various establishments throughout the world, although possibly derived from cowpox, horsepox, or variola, are very much alike and are all referred to as vaccinia. These strains have been subjected to more detailed laboratory investigation than probably any other virus. Vaccinia has a wide host-range and can be propagated in series, not only on the skin of calves and sheep in the preparation of lymph but in the common laboratory animals. The lesions are histologically similar to those caused by variola virus in man; but in man vaccinia is less virulent, rarely producing a generalized skin eruption. Although strains of vaccinia may have been derived from the natural pox disease of cows or horses, repeated propagation in vaccine lymph institutes has so modified them that they exhibit some characteristics not possessed by recently isolated strains of cowpox virus. This is referred to below.

Variola as a Source of Vaccine

In the belief that cowpox was essentially an infection of the cow by variola virus many attempts were made last century to infect cows with smallpox material. Most of these attempts were unsuccessful. Sometimes papular lesions appeared on the skin at the site of inoculation, but these could not be carried on in series, and when material from these papules was used to inoculate children smallpox, not vaccinia, resulted. The work on this subject was reviewed by Copeman in 1899 and more recently by Horgan (1938). A few workers claimed success; among them Ceely, who, after many failures, recorded in 1840 details of two successful experiments made with matter from seventh- or eighth-day smallpox pustules. From the vesicles which appeared on the inoculated cows children were vaccinated, and the lymphs from these were widely used with apparently good results. There must, however, remain some doubt about the nature of the virus which Ceely recovered from the cows. For in his first animal standard vaccine was injected in the neighbouring skin the day before a vesicle appeared at one of the sites of inoculation of variola fluid. His second successful animal was inoculated with smallpox vesicle fluid at a time when vaccine vesicles had developed at the vaccination sites in the first cow.

Badcock (1845), who inoculated 90 cows with smallpox material during a period of four years, used the lymph from occasional successful cases for the vaccination of children, and his lymphs were widely distributed. Details of Badcock's experimental procedure are not available. In later apparently successful experiments on the development of vaccinia from variola several transfers in the skin of the cow were necessary, as in the experiment of Copeman. Most French workers failed to obtain vaccinia from cows or rabbits inoculated with smallpox material. The successful results obtained occasionally by others have practically all been achieved in vaccine institutes, where the possibility of contamination with vaccinia can rarely be excluded. The observations of Kelsch and his colleagues (1909, 1910) showed the contagious nature of vaccinia for the cow. They found that, in a vaccine lymph institute, cows which had been inoculated in the scarified skin only with glycerin developed some days later a few vesicles which proved to be vaccinial. More recently the liability of rabbits to be infected with minimal vaccinial lesions when kept near experimentally infected animals has been recognized.

The monkey is the only experimental animal which can be readily infected with both variola and vaccinia viruses, and in the monkey variola apparently remains variola. But when variolous matter from the monkey is passed to the rabbit a vaccinial mutant is said to appear in this animal after several transfers. The

emergence of vaccinia is apparently facilitated by intratesticular infection followed by inoculation of the testicular material on the scarified skin of fresh animals. Vaccinial strains were claimed to have been derived in this way by Amies in 1932 (personal communication) and by Horgan (1938), who took precautions to avoid the introduction of vaccinia from extraneous sources. The vaccinial strain obtained by Amies was later used for the preparation of vaccine lymph by Horgan (Horgan and Haseeb, 1945).

Variola strains do not apparently give rise to vaccinial mutants during prolonged cultivation on the chorio-allantois of chick embryos. Virus propagated in this tissue may multiply to some extent during repeated transfers in the testes of rabbits, but infectivity for the rabbit skin is not acquired (Nelson, 1943). Our own experience with a strain of variola in the form of crust extract or infected chorio-allantois and with egg-cultured alastrim virus has so far been similar to Nelson's. Both strains of virus multiplied in the testes of rabbits through several transfers without obvious clinical evidence of inflammatory reaction; but lesions on the skin reproducible in series could not be obtained by dermal inoculation of testicular material. Nor did the lesions on the chorio-allantois produced by virus from the testes of successive rabbits show any change towards the vaccinial type.

The role of monkey passage in the reported emergence of a vaccinial variant is not clear. That infection of the skin of the monkey merely increases the possibility of a vaccinial mutant emerging through increase of dose of virus to be inoculated in the rabbit seems unlikely; for direct inoculation of fresh human vesicle fluid rich in variola virus or of heavily infected chorio-allantoic suspension does not facilitate the appearance of vaccinia in rabbits. It may be that for the appearance of a typical vaccinial mutant more than one mutational step is necessary, and the first of these may take place in the skin of the monkey. Growth in the testis of the rabbit may provide suitable conditions for the emergence of further mutation, and the final step may occur as a result of the selective environment in the rabbit skin. The numerous failures to produce vaccinia by direct inoculation of smallpox virus from man to the skin of the rabbit or of the cow suggest that these tissues are so unfavourable to the continued growth of the human virus that there is no opportunity for the mutational steps necessary for the appearance of vaccinia.

The strain of vaccinia virus used for the routine preparation of lymph in this country is believed to have been derived from a case of smallpox in Cologne during the last century (McClean, personal communication), and one of the strains currently used in Uganda is said to be of variolous origin.

It seems, then, that vaccinia now used may be far removed from the cowpox of Jenner. What are the characters of cowpox virus recently derived from the natural infection in cattle, and how do they compare with those of vaccinia and variola viruses? I propose to consider briefly recent work bearing on this question.

Cowpox at the Present Time

Donaldson and Waldron (1951) state that only eight outbreaks of cowpox had been reported in this country during the last 50 years, although they believe that the disease is more prevalent than this suggests. This is certainly our own experience. From 1944 to 1950 we have examined material from 10 different outbreaks of cowpox in different parts of England and Wales, and in each instance investigation of these incidents was occasioned by the affection of milkers. From this material eight strains of cowpox virus have been isolated, mostly from the human lesions. Outbreaks of cowpox therefore seem to be as common now as in Jenner's day, though smallpox is no longer an endemic disease. Nor is there any evidence that the disease in cattle originates from contact with recently vaccinated individuals.

Although the first description of the disease is contained in Jenner's *Inquiry*, it seems likely that it had existed for many years previously. Cowpox is milder than the pock diseases of other animals; the lesions are confined to the teats and udders, spread within a herd being effected mainly by the manipulations during milking. The nature and history of the disease and the characters of the virus indicate that cowpox is an infection peculiar to the cow. It seems that the infection, apart from the process of milking, might often be latent. The mild nature of the lesions in the cow and the possibility that the disease is kept going by the persistence of trivial infection in immune animals, as in herpes simplex infection in man, might be regarded as evidence that cowpox in cattle has a very long history.

The disease now to be seen in cows and that contracted by milkers conforms to its first description by Jenner and to the later detailed account of Ceely (1840). The lesions in milkers usually occur on the hands, often between the thumb and first finger, but may be seen on the forearm or face. In unvaccinated persons the disease generally runs a more severe course than that which follows primary vaccination in adults (Davies, Janes, and Downie, 1938), and the local lesion is often associated with lymphangitis, lymphadenitis, and some degree of fever and general upset. Healing of the lesions may take several weeks, but fatal infections have not been recorded.

The appearance of the vesicles on human skin is similar to that of vaccination vesicles, although there is more congestion and the contents may be blood-stained. This tendency to haemorrhage was noted by Jenner and by Ceely in the vesicles of cows and of milkers. Histologically, the cowpox vesicle has the same general appearance as the vaccination and smallpox vesicle. In the epithelial cells at the base of the lesion, however, in suitably stained sections there are strongly acidophilic compact intracytoplasmic inclusions which differ from the inclusions of the vaccinia or variola lesion. Laboratory animals and developing chick embryos can readily be infected with vesicle fluid from human lesions. The animal pathogenicity and experimental host range of cowpox virus is similar to that of current strains of vaccinia and is less restricted than that of variola virus. The lesions in experimentally infected animals always have a haemorrhagic character, which is not a feature of lesions caused by dermal strains of vaccinia. In skin epithelium and in mesodermal cells, including vascular endothelium of the underlying cutis, the typical cytoplasmic inclusions are constantly found (Downie, 1939).

Immunological Relationship between Cowpox, Vaccinia, and Variola Viruses

It has been shown by various workers that, in animals, infection with cowpox or with vaccinia virus produces immunity of similar degree against both viruses. Sera

from animals immunized against either virus neutralize both viruses in the rabbit skin, but minor serological differences have been elicited by cross-absorption of immune sera with the two viruses. Cowpox virus removes from an antivaccinial serum agglutinating, complement-fixing, and neutralizing antibody for cowpox more readily than it removes corresponding antibody for vaccinia virus; the converse holds for the absorption of cowpox antiserum with vaccinia virus.

Variola virus cannot be used for comparative immunological studies in the usual experimental animals because of its very limited pathogenicity; such studies made in monkeys have shown immunological similarity between strains of vaccinia, variola, and alastrim (see Gordon, 1925; Horgan and Haseeb, 1939). Variola and alastrim viruses can, however, be readily propagated on the chorio-allantois of developing chick embryos, where they cause typical focal lesions which are different from those produced by vaccinia and cowpox. In Liverpool my colleagues and I have made serological studies of these viruses, using human convalescent sera and virus preparations from smallpox crusts or from infected chick chorio-allantois. Experiments have also been carried out with immune sera prepared in fowls by injections of virus propagated in chick membranes. By complement fixation and inhibition of complement-fixation techniques the viruses of alastrim and variola could not be differentiated. Vaccinia virus was also closely related. There was considerable cross-reactivity between cowpox virus and the variola-vaccinia group, but this virus showed more divergence from variola than did vaccinia (Downie and Macdonald, 1950).

In neutralization tests on the chorio-allantois, using human convalescent and animal immune sera, immunological differences between these viruses could not be readily demonstrated by the usual technique. The use of absorbed sera elicited minor antigenic differences of a nature similar to those shown by the *in vitro* techniques (Downie and McCarthy, 1950). Recently we have tested the cross-neutralizing power of convalescent sera from three unvaccinated smallpox patients and from three unvaccinated persons who had recovered from cowpox infection contracted from cattle. The cowpox virus used had been isolated from a cow and passed three times on eggs, and the variola strain from smallpox crusts had been passed five times on eggs. The results (see Table) showed that the smallpox convalescent sera

Neutralization of Cowpox and Variola Virus by Convalescent Sera from Cowpox and Smallpox Patients

Convalescent Sera	% Reduction of Virus Lesions on Chorio-allantois	
	Cowpox Virus	Variola Virus
Cowpox 1	73	74
,, 2	93	84
,, 3	89	77
Smallpox 1	88	95
,, 2*	80	44
,, 3	89	93

* Serum taken on eighth day of illness.

neutralized both viruses, and the sera from the cowpox patients neutralized variola virus practically to the same degree as they neutralized cowpox virus. The results with these sera from unvaccinated persons confirm the immunological similarity between cowpox and variola virus; a finding which supports Jenner's contention that those who have suffered from cowpox are thereby rendered immune to smallpox.

In summarizing our knowledge of these three viruses we can say that there is a close immunological relationship between the viruses of variola, the natural pock disease of man, and cowpox, the natural pock disease of bovines, although the diseases are clinically and epidemiologically so different. Variola is an acute generalized infection, highly contagious, whereas cowpox is mild with only a local eruption and is not contagious. The skin lesions in the two diseases are histologically similar, although those of cowpox are more constantly haemorrhagic and the virus inclusions are different in appearance. The virus of variola is much more limited in its experimental host range, being infective for the monkey and the chick chorio-allantois but not readily causing infections reproducible in series in other animals.

Strains of the artificially propagated vaccinia virus are immunologically related to both variola and cowpox virus. It is practically identical in this respect with variola and shows minor serological differences from cowpox. The lesions produced by vaccinia in the skin of man and animals are histologically identical with those produced by variola in human skin, and the inclusion material has the same appearance. On the other hand, vaccinia strains resemble cowpox virus in that they have the same wide experimental host range and in man do not usually produce generalized skin eruptions and are not contagious. The differences between cowpox and vaccinia viruses do not seem to be fundamental, and it seems possible that by the repeated artificial propagation of cowpox virus in animals or on the skin of man a virus with the characters of vaccinia could emerge.

Conclusion

In a recent publication Professor Kaiser (1949) laments: "That the English are now discarding [*ablehnen*] the life work of one of their most famous sons is a tragedy that we can only note without comment." But we have not discarded Jenner's work. Although compulsory vaccination has recently been abolished in this country because of the greatly lessened risk of smallpox, a risk lessened in some measure by Jenner's labours, we still recognize the great value of vaccination in protecting those exposed to infection; and Jenner's vaccination is an essential part of the procedure adopted to prevent the spread of smallpox in this country when infection is introduced from abroad. Greenwood (1935), after a critical discussion of the statistical evidence on the value of vaccination in lessening the ravages of smallpox, concludes that Jenner was, directly or indirectly, the means of saving many hundreds of thousands of lives; a conclusion, he submits, quite enough to entitle Englishmen to take pride in the recollection that Jenner was their countryman.

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IDIOPATHIC HYPOCHROMIC ANAEMIA IN YOUNG ADULT MALES

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Idiopathic hypochromic anaemia is described by Whitby and Britton (1946) as a chronic anaemia chiefly found in middle-aged women and characterized by a low mean corpuscular haemoglobin concentration and mean cell volume; achlorhydria and glossitis are usual, while koilonychia is common. Attention was first drawn to the condition by Faber (1913) and since that time ample descriptions of the disease in women have appeared in the literature.

According to Whitby and Britton the disease is uncommon in males, while Wintrobe (1946) states that 4% of cases are found in men. Faber's original account of 22 cases contained three males. Witts (1930a) analysed a series of 50 cases, one of which was a man; while Davies (1931a) later reviewed the subject of achlorhydria and anaemia and found no males in a series of 15 cases of hypochromic anaemia. In a further series recorded by Davies (1931b) there were four males in a total of 55 cases. Parkes Weber and Weisswange (1933) described four cases of anaemia of unexplained origin occurring in men, only two of which were of the true hypochromic type. Bethell *et al.* (1934) found two males in a series of 33 cases; Britton (1936) recorded four cases of idiopathic hypochromic anaemia occurring in men in a series of 66. Reviewing the incidence of chronic nutritional anaemia, Davidson and Fullerton (1938) found no cases in a series of 167 adolescent and adult males, while the Medical Research Council (1945) showed that between 2 and 3% of adult males had a haemoglobin level below 80%, and 0.2% of adolescent males under the age of 20 years had a haemoglobin level below 70%. In that survey no cause was apparently sought for the anaemia.

The occurrence of idiopathic hypochromic anaemia in the *young* adult male is, however, very rarely described. Wintrobe states that of the cases occurring in men, 82% are found between the ages of 20 and 50 years. Thomson (1943) recorded nine cases occurring in adolescent males whose ages ranged from 17 to 19 years, and Beckert (1938) described two cases of apparent chlorosis in youths aged 16 and 17. The five cases of chlorosis recorded by Witts (1930b) were found in young men with ages varying from 18 to 28 years, while of the series of 26 cases of idiopathic hypochromic anaemia in males described by Witts and Burger (1934) eight were males below the age of 30.

The present series of 20 cases in young soldiers has been seen by us over the course of the past two years at the Cambridge Military Hospital, Aldershot. Although the ages of patients (all male) attending the hospital range from 18 to 60 years, cases of *idiopathic* hypochromic anaemia have been observed only in soldiers from 18 to 23 years of age. All but one of the cases were found in men with less than three months' service, and an interesting point for which we can offer no explanation is that of the 20 patients 11 came from the Royal Army Ordnance Corps. In none was there any relevant past history, and in one case only was there any familial history of anaemia. This man had an anaemic brother. On close questioning no abnormal food habits were found. Clinical examination and special investigations revealed no evidence of gross organic disease such as chronic infection, gastro-intestinal disorders, chronic nephritis, recurrent rheumatism, or neoplasm. A particular search for gastro-intestinal haemorrhage or bleeding haemorrhoids failed to disclose a cause for the anaemia.

A summary of the main clinical findings is shown in Tables I and II. Some representative case histories are given below.

Case 5

Aged 19. Service, one week. Civilian occupation, plasterer's labourer. History: was examined one year previously by civilian medical board and call-up deferred owing to anaemia; not investigated, but advised to take iron tablets, which he did not do; no symptoms before joining Army, but marked dyspnoea on exertion since recruitment; had "gastritis" five years previously; no relevant family history. Physical examination: mucous membranes very pale; sparse axillary and pubic hair, fine in quality; skin thick and dry, nails fluted; tongue, teeth, and pharynx healthy; spleen just palpable; no haemorrhoids.

Investigations.—Hb, 7.6 g.% (Sahli); R.B.C., 5,000,000; C.I., 0.52; P.C.V., 32%; M.C.V., 64 μ^3; M.C.H., 15.2 $\mu\mu$g.; M.C.H.C., 23.7%; W.B.C., 6,400 (P. 54%, L. 42%, M. 2%, E. 2%); red-cell fragility within normal limits; chest radiograph normal; F.T.M., histamine-fast achlorhydria; stools, negative for O.B. (six specimens).

Treatment: ferrous sulphate, 6 gr. (0.4 g.) t.d.s.; dilute HCl, 15 min. (0.9 ml.) t.d.s., a.c. Result: Hb, 14.2 g.%; R.B.C., 4,800,000; C.I., 1, after 11 weeks; no return of symptoms after two years.

Case 9

Aged 18. Service, four weeks. Civilian occupation, plumber's mate. History: had noticed marked dyspnoea and palpitations on exertion for three months; more severe since joining Army; had always been pale; appetite good, no abdominal pain, bowels opened regularly; no relevant past or family history. Physical examination: slightly built; pallor of skin and mucous membranes; nails thin and transversely ridged; tongue, teeth, and pharynx healthy; soft systolic murmur localized to mitral area; tip of spleen easily felt. Liver just palpable. No haemorrhoids.

Investigations.—Hb, 8.8 g.% (Sahli); R.B.C., 4,700,000; C.I., 0.69; P.C.V., 35%; M.C.V., 74 μ^3; M.C.H.C., 25%; stained film of red blood cells showed marked anisocytosis and poikilocytosis, but no polychromasia or stippling; W.B.C., 8,800 (P. 49%, L. 50%, M. 1%); reticulocytes, 0.5%; fragility of red blood cells, within normal limits; blood bilirubin, 0.3 mg./100 ml.; F.T.M., complete achlorhydria; stools, three specimens negative for O.B.; chest radiograph normal; barium meal normal. The fact that this man had worked with lead as a plumber's mate for three years may have contributed to the production of the anaemia. But there were no other symptoms or signs suggestive of lead-poisoning. The presence of a normal red-cell fragility and a normal serum-bilirubin level, together with the absence of stippling, make it extremely unlikely that the anaemia was a toxic manifestation of lead.

Treatment: ferrous sulphate, 6 gr. t.d.s., dilute HCl 15 min. t.d.s., a.c. Result: Hb, 12.6 g.%; R.B.C., 5,400,000; C.I., 0.8 after eight weeks; no return of symptoms after 18 months.

Case 6

Aged 18. Service, four weeks. Civilian employment, shop assistant. History: marked dyspnoea on exertion since joining Army; had previously felt quite fit; no relevant past or family history. Physical examination: poor physique; skin dry and coarse; marked pallor of mucous membranes; pharynx, teeth, and tongue healthy; no koilonychia; liver and spleen not felt: no haemorrhoids.

Investigations.—Hb, 6.9 g.% (Sahli); R.B.C., 4,240,000; C.I., 0.57; P.C.V., 27%; M.C.V., 66 μ^3; M.C.H., 16.2 $\mu\mu$g.; M.C.H.C., 25.3%; W.B.C., 7,600 (P. 53%, L. 42%, M. 3%, E. 1%, B. 1%); reticulocytes, 2%; red-cell fragility within normal limits; chest radiograph normal; F.T.M., complete achlorhydria with slight histamine response; stools, negative for O.B. (five specimens, first specimen weakly positive); barium meal normal; Kahn test negative.

Treatment: ferri et ammon. cit., 40 gr. (2.6 g.) t.d.s., dilute HCl, 15 min. t.d.s., a.c.; "multivite" tablets, 1 t.d.s. Result: Hb, 11.2 g.%; R.B.C., 5,000,000; C.I., 0.78 after 10½ weeks; no return of symptoms after two years.

Case 13

Aged 20. Service, three weeks. Civilian occupation, farm labourer. History: vague epigastric ache present spasmodically for previous four weeks, unrelated to food; appetite good; no vomiting; bowels opened regularly; no melaena; dyspnoea on exertion; no relevant past or family history. Physical examination: marked pallor of skin and mucous membranes; koilonychia; tongue, teeth, and pharynx healthy; liver and spleen not felt; no haemorrhoids.

Investigations.—Hb, 9.5 g.% (photoelectric); R.B.C., 5,200,000; C.I., 0.62; W.B.C., 4,500 (P. 50%, L. 31%, M. 15%, E. 4%); fragility of red blood cells within normal limits; chest radiograph normal; F.T.M., hypochlorhydria; stools, negative for O.B. (three specimens).

Treatment: ferrous sulphate, 6 gr. t.d.s., dilute HCl, 15 min. t.d.s., a.c. Result: Hb, 14.7 g.%; R.B.C., 5,250,000; C.I., 0.97; quite fit after 11 months.

Comments on Table I

The duration of the symptoms was short in all cases. The commonest complaint was of dyspnoea; 15 of the cases complained of some degree of undue breathlessness on exertion. The severity of the dyspnoea did not appear to bear any constant relation to the degree of anaemia. In only three instances were there dyspeptic symptoms, consisting of epigastric pain. Bloated feeling after food, dysphagia, and diarrhoea, symptoms often found with achlorhydria, were not encountered. In common with Witts and Burger (1934) we observed a definite tendency to immaturity, all appearing some few years younger than their actual ages. This immaturity and the "sneaking college look" (Wycherley, 1672) may have, albeit unconsciously, prompted the personnel selection officer in his choice of posting for these men.

There was no tendency to eunuchoidism or underdevelopment of the genitalia, which Gardiner-Hill (1931) and Filo (1933) associate with anaemia. The patients' skins were smooth, and the hair fine; acne was absent in all cases. Glossitis and soreness of the tongue were

TABLE I.—*Main Clinical Findings*

Case No.	Age	Symptoms		Physical Signs			
		Dyspnoea	Other Symptoms	Pallor	Splenomegaly	Apical Murmurs	Miscellaneous
1	18	Nil	Nil	Marked	—	—	Poor physique
2	18	Mild	Would-be blood donor. Anaemia discovered on routine blood examination	Slight	—	—	—
3	18	Severe	Nil	Marked	—	—	Immature
4	18	Mild	Lassitude. Generally unwell	,,	—	—	—
5	19	Severe	Anaemia noted by civilian medical board; enlistment deferred	,,	Palp.	Systolic	Nails fluted; skin hard and dry; pubic hair scarce
6	18	,,	Nil	,,	—	—	Poor physique
7	18	Mild	Pains in calves on exercise	,,	—	Systolic	Poor physique; koilonychia; dental sepsis
8	18	Nil	Headaches	,,	—	—	Koilonychia
9	18	Severe	Palpitations	,,	Palp.	Systolic	Poor physique; nails thin; transversely ridged; liver palpable
10	18	Mild	Occasional pins-and-needles in feet	,,	—	—	No abnormal C.N.S. signs
11	23	Severe	Attacks of dizziness	,,	—	—	—
12	18	Nil	Epigastric pain not related to meals	,,	—	—	—
13	20	Mild	,, ,, ,, ,,	,,	—	—	Koilonychia
14	18	Marked	Would-be blood donor. Anaemia discovered on routine blood examination	,,	—	—	Poor physique
15	18	Mild	Nil	,,	—	—	,, ,,
16	18	Nil	Epigastric pain. Palpitations	,,	—	Systolic	,, ,,
17	18	,,	Would-be blood donor. Anaemia discovered on routine blood examination	,,	—	—	—
18	20	Severe	Lassitude, headaches, dizziness	,,	Palp.	—	Liver palpable
19	18	,,	Lassitude, headaches	,,	—	Systolic	Nails flattened; poor physique
20	20	,,	Nil	,,	Palp.	,,	Poor physique; gross koilonychia

not seen and oral sepsis, so beloved of the elder clinician, was in no case a marked feature. Changes in the nails were present in seven cases, frank koilonychia in four, brittleness and fluting in three. Witts and Burger (1934) described no changes in the nails, whereas Thomson (1943) found 4 with changes in 10 cases. In Case 20 the koilonychia was gross, the depression in the thumbnail holding eight drops of water. Splenomegaly was found in four of our cases. This proportion is similar to that described by Witts and Burger (1934). In Thomson's cases, however, the spleen was enlarged and palpable in 5 cases out of 10. These observations are to some extent in agreement with those of Witts and Burger (1934) in that "the typical syndrome of hypochromic anaemia as it appears in women with microcytic anaemia, achlorhydria, splenomegaly, and dystrophic changes in the tongue, the pharynx, and the nails is rarely encountered in the adult male."

Comments on Table II

The haemoglobin levels are expressed as grammes per 100 ml., and were estimated either by the methods of Haldane or Sahli, or by means of a photoelectric colorimeter standardized against the Gibson–Harrison artificial standard. The figure of 14.5 g. per 100 ml. was taken as 100% for the purposes of colour-index calculation. The fractional test meals were performed using 50 ml. of 7% ethyl alcohol as the primary stimulus, with the addition in some cases of 0.5 mg. of histamine subcutaneously.

Examination of the stained films invariably revealed variations in shape, size, and colour of the red blood cells, in some cases out of proportion to the degree of the anaemia. Red-cell fragility and platelet and reticulocyte counts were within normal limits. The leucocyte counts varied between 4,000 to 10,000 per cm., and most cases showed some degree of neutropenia. Chest radiographs showed no evidence of pulmonary or cardiac disease, and the examinations of stools for occult blood were without significant exception negative.

Thirteen cases showed complete achlorhydria. Normal gastric acidity was present in Case 17 and hyperchlorhydria was demonstrated in Cases 14 and 16. In none of these was there any radiological evidence of gastric or duodenal abnormalities. The remaining case with hyperchlorhydria did not have a peptic ulcer excluded radiologically, but examinations of the stools for occult blood were consistently negative. These cases of hypochromic anaemia associated with a normal or high gastric acidity are presumably examples of the chlorotic type of anaemia seen more often in former days in adolescent females.

Treatment

Treatment was conducted on routine lines with the patients at rest in bed on a normal diet. All cases were given iron preparations in the form of ferrous sulphate, 6 gr. (0.4 g.) t.d.s., or ferri et ammon. cit. 40 gr. (2.6 g.) t.d.s., together with vitamin supplements. Those with achlorhydria were given dilute HCl 15 min. (0.9 ml.) t.d.s., in addition. Patients were advised to continue treatment after discharge from hospital.

The results of treatment as indicated in Table II were in most cases satisfactory. The patients have been

TABLE II

Case No.	Hb g.%	R.B.C. (mils.)	C.I.	P.C.V. %	M.C.V. (μ³)	M.C.H.C. %	W.B.C. Diff. %	Comment on Film	F.T.M.	Results of Treatment			Duration of Treatment
										Hb	R.B.C.	C.I.	
1	7·87 (H)	4·1	0·66	33	80	24	8,400 P58, L36, M2, E4	Hypochromia, anisocytosis, poikilocytosis	Achlorhydria	14·7	5·3	0·93	8 weeks
2	9·4 (S)	3·83	0·84	36	94	26	7,800 P64, L32, M3, E1	,,	,,	14·5	5·2	0·95	6 ,,
3	6·8 (S)	3·62	0·65				7,300 P69, L29, M1, B1	Anisocytosis, polychromasia	Histamine-fast achlorydria	14·0	5·35	0·90	6 ,,
4	8·0 (H)	4·06	0·69				6,700 P54, L36, M5, E5	Hypochromia, anisocytosis, poikilocytosis	Achlorhydria	13·8	5·02	0·91	6 ,,
5	7·6 (S)	5·0	0·52	32	64	23·7	6,400 P54, L42, M2, E2	Gross anisocytosis and poikilocytosis, hypochromia	Histamine-fast achlorhydria	14·2	4·8	1·0	11 ,,
6	6·9 (S)	4·24	0·57	27	66	25·3	7,600 P53, L42, M3, E1, B1	Hypochromia, anisocytosis, poikilocytosis	Achlorhydria, slight histamine response	11·2	5·0	0·78	10 ,,
7	7·29 (H)	4·15	0·60	30·5	73·5	23·9	6,000 P70, L26, M3, E1	,, ,,	Achlorhydria	14·17	5·0	0·98	12 ,,
8	7·87 (H)	3·96	0·68				5,200 P30, L59, M11	Hypochromia, anisocytosis	,,	12·0	5·3	0·77	4 ,,
9	8·8 (S)	4·70	0·69	35	74	25	8,800 P49, L50, M1	Anisocytosis, hypochromia, poikilocytosis; no stippling	,,	12·6	5·4	0·80	8 ,,
10	7·9 (P)	4·75	0·57				7,600 P55, L37, M4, E3, B1	Anisocytosis, poikilocytosis	,,	12·6	5·0	0·87	6 ,,
11	10·4 (S)	5·0	0·72				6,800 P60, L35, M4, E1	Red cells appear normal	,,	13·7	4·84	0·97	7 ,,
12	7·7 (S)	4·18	0·63				8,200 P57, L40, E2, M1	Marked hypochromia some polychromasia	Hyperchlorhydria	12·9	4·9	0·90	6 ,,
13	9·45 (P)	5·2	0·62				4,500 P45, L50, M3, E2		Hypochlorhydria	14·7	5·25	0·97	6 ,,
14	8·37 (H)	3·5	0·80				7,000 P58, L39, M2, E1		Hyperchlorhydria	13·1	4·93	0·9	5 ,,
15	8·0 (H)	3·61	0·77	30	83·3	26·6	7,000 P60, L26, M8, E6	Hypochromia, anisocytosis, poikilocytosis	Achlorhydria	13·8	5·6	0·85	6 ,,
16	8·2 (P)	4·48	0·65	34	75·5	23·1	9,100 P72, L25, M3	,, ,,	Hyperchlorhydria	14·2	5·2	0·93	8 ,,
17	9·66 (H)	4·8	0·70	40	84	24·1	8,200 P69, L26, M4, E1	Anisocytosis, hypochromia	Normal acidity	15·66	5·0	1·1	5 ,,
18	10·3 (H)	5·0	0·71	36	92	22·4	7,200 P65, L30, M3, E2	Hypochromia	Histamine-fast achlorhydria	14·3	5·2	0·9	4 ,,
19	11·0 (P)	5·0	0·75				9,000 P72, L25, M3	Sl. anisocytosis and poikilocytosis	,, ,,	16·0	5·0	1·1	5 ,,
20	6·3 (S)	3·5	0·60				7,800 P60, L32, M4, E3, B1	Anisocytosis, hypochromia, poikilocytosis	,, ,,	14·5	5·3	0·92	10 ,,

H = Haldane. S = Sahli. P = Photoelectric colorimeter.

followed up for periods varying from three months to two years, and, although it has not been possible to obtain follow-up blood pictures, in no cases have symptoms returned.

Discussion

The fact that these cases of anaemia are labelled idiopathic indicates that their aetiology is obscure. A combination of factors has probably rendered insufficient the amount of iron available for haemoglobin synthesis. It is less likely that there was an excessive iron loss by way of chronic haemorrhage, although the possibility that this had occurred in the past cannot be ruled out. The deficiency of hydrochloric acid in the gastric secretions was probably one of the determining factors, but it cannot have been the primary cause, as four of the patients were not achlorhydric. Also, as noted by Davidson and Fullerton (1938), not all achlorhydric people are anaemic, and, whereas the incidence of achlorhydria increases with advancing years, idiopathic hypochromic anaemia in old people is rare.

The possibility that the anaemia in Case 9 was a toxic manifestation of lead has already been considered. We have also pointed out that all but one of the men had less than three months' service. Probably the amount of extra physical exertion involved in their basic training was sufficient to produce symptoms in subjects previously anaemic but hitherto symptomless. This certainly was true of Case 20, in which the gross degree of koilonychia was evidence of a long-standing anaemia, and also of Case 5, in which an anaemic state had been demonstrated twelve months previously.

There is, however, a further possible explanation. Cantarow (1947) states that 23% of the minimal iron intake is required for the manufacture of muscle haemoglobin and for use in muscle and other parenchymal cells. This iron is not available for blood haemoglobin formation, and blood haemoglobin may constitute an important source of iron necessary for growth. Davidson *et al.* (1933) have shown that persons with achlorhydria exist on an intake of iron which is very near the borderline. In most cases the first few months of the recruits' lives in the Army are accompanied by a marked increase in weight, due, in part, to enhanced development and hypertrophy of the musculature. This change is more pronounced in those previously immature and of poor physique. It may be that this abnormal demand for iron cannot be met by increased intake, on account of impaired absorption from the gut, and iron for the enhanced development is obtained at the expense of the blood haemoglobin. Thus either an anaemic state is produced or a latent anaemia is rendered obvious.

Summary

An account is given of 20 cases of idiopathic hypochromic anaemia occurring in young men.

The majority of cases showed a definite tendency to immaturity, and nail changes were present in some. The typical syndrome of hypochromic anaemia as it occurs in women was not seen.

Achlorhydria or hypochlorhydria was present in 16 of the cases. Of the remainder, normal gastric acidity was present in one and hyperchlorhydria in three.

The blood pictures rapidly improved, and in most cases became normal on treatment with adequate amounts of iron.

There was no indication that the anaemias were the result of blood loss. They were probably due to an increased demand for iron coupled with defective intestinal absorption.

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ORAL HEXAMETHONIUM BROMIDE IN ESSENTIAL HYPERTENSION

BY

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The group of compounds known for convenience as methonium halides emerged in the course of a systematic search for synthetic substitutes for curare. The pharmacological researches of Paton and Zaimis (1949) showed that compounds with carbon chains of intermediate length (five or six atoms) exert their action at ganglionic synapses rather than at neuromuscular junctions and that they are capable of influencing profoundly the functions of the autonomic nervous system. An opportunity was thus provided for a new approach to the management of diseases, such as peptic ulceration and essential hypertension, in which hyperactivity of the autonomic nervous system might be conceived to play a part.

These drugs are stable and soluble, and are apparently absorbed freely unchanged from the alimentary tract. As soon as adequate amounts became available Kay and Smith (1950), working on peptic ulcer, showed that hexamethonium bromide is pharmacologically active when given orally. We were fortunate in having direct access to Kay and Smith's work in progress. It seemed to suggest the possibility that a simple effective method might be devised of controlling by oral drug therapy the manifestations of essential hypertension. A clinical investigation along these lines was begun early in 1950. As the methonium drugs are now freely marketed we feel it appropriate that we publish our results and attempt to indicate provisional tentative conclusions.

Our material consists of 15 cases of essential hypertension under treatment for periods varying from ten months to one month. The latter short period refers to one case of malignant hypertension (Case 15) which did not yield to methonium drugs. The patient was submitted to surgery and died. Most of the others (cases of severe hypertension in the benign phase) have come under treatment because of disabling symptoms. Apart from such brief periods in hospital as were necessary for investigation and assessment, these have been treated on an out-patient basis, and the aim has been to keep them not less active than they were before treatment began. Particulars of age, sex, and duration of treatment are listed in Table I. In addition, for convenience, an indication is given in this table of the general results achieved.

TABLE I.—*List of Cases and General Assessment of Results*

Case No.	Age	Sex	Duration of Therapy	Result
1	29	F	10 months	Improved
2	50	F	9 "	I.S.Q.
3	51	F	8 "	Worse
4	35	M	8 "	Improved
5	62	F	7 "	"
6	57	M	7 "	I.S.Q.
7	34	M	7 "	Improved*
8	43	M	7 "	Worse
9	44	F	7 "	Improved
10	47	M	7 "	I.S.Q.
11	49	F	6 "	"
12	65	F	3 "	"*
13	27	F	3 "	"
14	45	F	2 "	"
15	27	F	1 month	Worse†

* Refused to persist owing to lack of subjective improvement.
† Malignant hypertension uncontrolled by C6 therapy; operation: death after second-stage total thoracic sympathectomy and splanchnicectomy.

Preliminary Investigations

Of the fifteen cases studied, thirteen were admitted to hospital for initial assessment. Some in fact had been under medical in-patient treatment for many weeks without response and were transferred to our care as potential subjects for surgery. The investigations carried out were those appropriate for cases of essential hypertension, and need not be fully detailed here. They included a thorough cardiovascular survey, assessment of renal function, and recording of fundal pathology. Lability tests were carried out with "sodium amytal," and in a few cases of violent and variable hypertension piperoxane tests were done to shed light on the possibility of the existence of phaeochromocytoma. Particular attention was naturally paid to estimation and recording of blood pressure, multiple readings being taken with the patient both erect and recumbent. In Tables II and III we have endeavoured to indicate a comprehensive clinical assessment by means of the groupings suggested by Palmer, Loofbourow, and Doering (1948). Changes in fundi, heart, and kidneys are graded 1–4. Fundal standards are those of Wagener and Keith (1939). Each case is given a P.L.D.* number representing the highest grade of damage found under any of the three headings.

Institution of Therapy

For short non-significant periods at the beginning of treatment of the earliest cases, pentamethonium (C5) was used alternately with hexamethonium (C6) (largely because the former drug was more readily available at that time) in an attempt to determine their comparative merits. These rather inadequate observations favoured C6, and the use of C5 was discontinued, especially because we quickly found that results in individual patients showed so much diurnal variability that intentional introduction of variables would render them insusceptible of analysis. The routine, therefore, has been to begin with test doses of C6 intramuscularly, the initial dose being 25 mg. If this proved ineffective, subsequent doses of 50 or even 100 mg. were given. This routine was designed to screen the cases for unusual sensitivity to the drug. It is in fact rather doubtful whether it is of value. The usual effect of intramuscular C6 is well known (Burt and Graham, 1950; Turner, 1950; Restall and Smirk, 1950). There is a sharp drop in blood pressure, maximal in about half an hour, with recovery over a period of 6 to 8 hours, the postural element in the hypotension persisting longest.

Following the test doses administered parenterally, oral therapy was begun. We found it most convenient to use tablets of 0.25 g. administered crushed, with water, before meals. At the same time the patients were made fully ambulant, and in most cases were discharged to the follow-up clinic within a few days. The commencing dose was 0.25 g. three times a day, before meals, and this was raised to a dosage adequate to lower blood pressure or, alternatively, to the maximum tolerable dose. In an "average" case the dosage stabilized at approximately 0.5 g. thrice daily, before meals.

Longer-term Assessment. — After discharge the patients were seen at regular intervals: Cases 1 and 9, for example, have been seen weekly without interruption for ten and seven months respectively. On each occasion they have spent the entire day at the hospital, where frequent blood pressure readings have been taken, renal status has been assessed, eye grounds have been examined, and, in addition, their general clinical condition has been objectively and subjectively evaluated. The other cases have been seen every few weeks.

Effects of Therapy

The pharmacological action of the methonium compounds is to diminish synaptic conduction throughout the autonomic nervous system and at adequate dosage to produce "synaptic blockade." The clinical effects of the operation of this mechanism must obviously be widespread, complex, and profound. There has been an understandable tendency to classify these effects in relation to the therapeutic objective of the investigator as primary effects and side-effects. Thus, if the investigation concerns peptic ulceration, lowering of blood pressure is a side-effect, while if hypertension is under consideration lowering of blood pressure becomes a primary effect and modification of the digestive processes is classified as a side-effect. We believe this differentiation to be unjustified. All the effects of methonium therapy seem to be predictable manifestations of the physiological action of the drugs. If the term "side-effect" is to be retained it can be only as a convenient abbreviation for effects inconvenient to patient and investigator.

Undesirable Effects

In the management of a case of essential hypertension the object of treatment is to lower the blood pressure and so to diminish strain on heart and blood vessels, especially the arterioles. It is probable that this can always be achieved by adequate amounts of the

*P.L.D. is used in the text and tables as a convenient abbreviation for Palmer, Loofbourow, and Doering.

methonium compounds. In addition, however, undesirable effects may be produced as a result of the actions of the drugs on either (*a*) the sympathetic, or (*b*) the parasympathetic.

(*a*) *Related to Sympathetic.*—Excessive lowering of blood pressure. It is common to have the patient complain of a certain amount of giddiness and lassitude. In effective dosage methonium drugs produce marked postural hypotension. In moderation this is therapeutically beneficial. When excessive, it may be completely incapacitating and result in the patient requiring to spend a day in bed. We have found patients to complain of dimness of vision at times when blood pressure is excessively low, apparently a pre-syncopal phenomenon. Marked postural tachycardia has not been observed. Our findings in this respect do not coincide with those of Restall and Smirk (1950). The hypotension produced by methonium therapy seems to differ strikingly from that following bilateral "Smithwick splanchnicectomy" and the comparison favours methonium. The absence of tachycardia may be explained by depression of the synapses of the cardiac ganglia.

(*b*) *Related to Parasympathetic.*—The effects on gastric secretion and motility are well known (Kay and Smith, 1950). In addition, all patients on effective dosage have relatively dry mouths and are constipated. In some there is progressive impairment of appetite culminating in anorexia. These modifications of alimentary function introduce difficulties in regulation of dosage, discussed more fully below. Almost all patients state that methonium therapy weakens the power of accommodation so that it may be difficult, for example, to read a newspaper. Two patients complained of dryness of skin and scalp.

Results

There is no doubt that in a condition such as essential hypertension final evaluation of any new method can be made only after many years of continuous work and careful recording of observations. We propose, therefore, to present our interim "results" only in quite general terms, and also to endeavour to analyse these in relation to a few of the more important elements in the clinical pathology of the condition.

As will be seen from Table I, five of our fifteen cases have been classified as improved, while the remaining ten are unchanged or worse. The improved cases are shown in synopsis in Table II. In this group the subjective satisfaction of the patients based upon relief of disabilities and complaints corresponds with recordable objective improvement, especially in the matter of reduction of blood pressure. In only one case has the P.L.D. grouping been lowered, by significant improvement in cardiac status resulting presumably from lowering of the blood pressure. The group is too small to permit classification in terms of age and sex. It is to be noted, however, that four of the five were comparatively young and that three of these four were cases of very severe hypertension, verging, as indicated by exudative phenomena in eye grounds or cerebrum, on the malignant phase. In Cases 1 and 9 these exudative phenomena slowly diminished under treatment, but not to a degree justifying lowering of P.L.D. group.

Therapeutic failures are outlined in Table III. There is no attribute which constantly differentiates these cases from those in Table II. The only general feature of the unsuccessful group is that dosage sufficient to affect the blood pressure produced disablement. Differences in tolerable dosage are rather striking. In Case 10, for

TABLE II.—*Synopsis of Improved Cases*

No.	Age and Sex	P.L.D. Group	Principal Complaint	Duration of Treatment	Final Maintenance Dose	Final P.L.D. Group	Subjective Change	Objective Change
1*	29 F	2	Headache, palpitation, and dyspnoea; retinal oedema	10 mths	0·75 g. t.i.d.	2	Improved	B.P. lowered
4†	35 M	3	Headache; encephalopathy	8 ,,	0.25 g. t.i.d.	3	Complaints relieved	B.P. lowered
5	62 F	3	Dyspnoea, headache, dizziness	7 ,,	0·75 g. t.i.d.	2	Complaints improved	B.P. lowered. Cardiac status improved
7	34 M	2	Headache, dizziness	7 ,,	0·75 g. t.i.d.	2	Complaints improved	B.P. lowered
9	44 F	4	Headache, dyspnoea, depression, papilloedema	7 ,,	0·5 g. t.i.d.	4	Complaints relieved	B.P. lowered. Retinopathy diminished

* Reported *in extenso*.
† Two months before institution of C6 therapy this patient had first-stage (right-sided) "Smithwick splanchnicectomy."

TABLE III.—*Synopsis of Unimproved Cases*

No.	P.L.D. Group	Principal Complaint	Duration of Treatment	Final Maintenance Dose	Final P.L.D. Group	Subjective Change	Objective Change
2	2	Headaches, dyspnoea	9 mths	0·5 g. t.i.d.	2	None	None with tolerable dose
3	3	Headaches, dizziness, slight dyspnoea	8 ,,	0·5 g. t.i.d.	3	Dyspnoea worse. Onset of angina	Development of cardiac failure
6	4	Headaches, recent episode of congestive failure	7 ,,	0·75 g. t.i.d.	4	Headaches less. Dyspnoea troublesome	Remains on verge of congestive failure
8	3	Headaches, angina, dyspnoea	7 ,,	0·5 g. t.i.d.	4	Headaches less. Angina less	C–V status I.S.Q. or worse. Early retinopathy
10	1	Lassitude, giddiness	7 ,,	0·125 g. t.i.d.	1	Lassitude increased	None with tolerable dose
11	2	Symptomless hypertension	6 ,,	0·25 g. t.i.d.	2	None	None
12	2	Giddiness, focal cerebral damage	3 ,,	0·5 g. t.i.d.	2	,,	Slight fall in B.P.
13	2	Slight dyspnoea slight angina	3 ,,	1·0 g. t.i.d.	2	Slight amelioration of symptoms	B.P. I.S.Q. E.C.G. slight improvement
14	2	Headaches, giddiness, dyspnoea	2 ,,	0·75 g. t.i.d.	2	Headaches and giddiness relieved. Slight dyspnoea persists	B.P. less*
15	4	Severe dyspnoea. Fundi Grade IV (K. & W.)	1 month	0·5 g. t.i.d.	4	None	Capricious effect on B.P.

* This case is recorded as unimproved, but the trend of her illness during C6 therapy appears to be in the direction of improvement.

TABLE IV.—*A Series of Sample Blood Pressures in 9 of the 15 Cases, Showing the Variable Effect*

Case No.	Average* B.P. Before Treatment		Lowest Single† B.P. Before Treatment		Lowest Single† B.P. on C6 Treatment		Highest Dose	Average‡ B.P. in Last Month of Treatment		Final Dose
	Upright	Recumbent	Upright	Recumbent	Upright	Recumbent		Upright	Recumbent	
1	—	230/140	—	200/120	130/80	145/75	1,000 mg. t.i.d.	170/97	185/85	2,000 mg. per day
3	—	214/118	190/105	200/110	200/130	185/100	750 ,, ,,	248/138	235/125	500 mg. t.i.d.
5	—	225/115	—	180/100	178/84	190/95	750 ,, ,,	161/95	186/103	750 ,, ,,
6	—	208/132	—	190/125	160/100	160/105	750 ,, ,,	227/139	229/143	750 ,, ,,
7	—	184/134	165/135	160/130	145/95	150/105	750 ,, ,,	163/125	165/125	750 ,, ,,
8	—	220/136	220/150	225/125	150/110	205/130	750 ,, ,,	201/142	230/139	500 ,, ,,
12	—	194/92	188/90	156/74	106/70	102/70	750 ,, ,,	166/105	177/103	500 ,, ,,
13	215/133	228/132	189/132	204/132	158/106	175/118	750 ,, ,,	186/135	193/135	1,000 ,, ,,
14	241/141	235/140	210/133	206/125	105/75	168/108	3,250 mg. per day	187/123	190/128	2,500 mg. per day

* These figures are the average of many recordings taken in the month before treatment and most closely represent the average level of the individual's blood pressure under standard conditions.

† These figures are the lowest blood pressure recorded before or during treatment and represent the lowest levels to which the pressures fell at any one time under these conditions.

‡ The figures in this column are those most nearly comparable to those in columns two and three.

example, it was never possible to give more than 0.125 g. of C6 thrice daily. The patient (a business man with no knowledge of the action of the drug he was taking) described himself as "completely knocked out" by this small dose, extremely weak, giddy, and almost unable to read. These effects are the more difficult to explain since the effect on his blood pressure was negligible. Case 13, on the other hand, received 3 g. a day with little effect on blood pressure and few added disabilities. In Case 15 the attempt to control malignant hypertension with C6 was abandoned after one month. The dosage used, at this early stage of our investigations, was not large (0.5 g. thrice daily), and the effects obtained on blood pressure were irregular. Operative treatment was followed by death from unexplained air embolism.

More Detailed Consideration of Effects of C6 Therapy

We have endeavoured to assess the results of C6 therapy in our small group of cases in terms of certain of the major manifestations of hypertensive disease.

Blood Pressure

The blood pressure of a hypertensive subject receiving C6 tends to show considerable variations in level, even in the course of a single day. The variations in systolic pressure tend to be much greater than those in the diastolic. A further element of variability is introduced by the effects of posture. Effective dosage with C6 produces a moderate reduction in the blood pressure in recumbency but a much more striking lowering of blood pressure taken in the erect posture. It is difficult to indicate in graphic or tabular form the effect of this therapy continued over a period of months. With these reservations, however, we have endeavoured to illustrate typical results by Table IV (Figs. 1*a*, 1*b*, and 2).

A conservative assessment of the effects of C6 therapy on blood pressure shows that a reasonably maintained lowering without clinical disablement has been achieved in eight of the fifteen cases. In the remainder the effect has

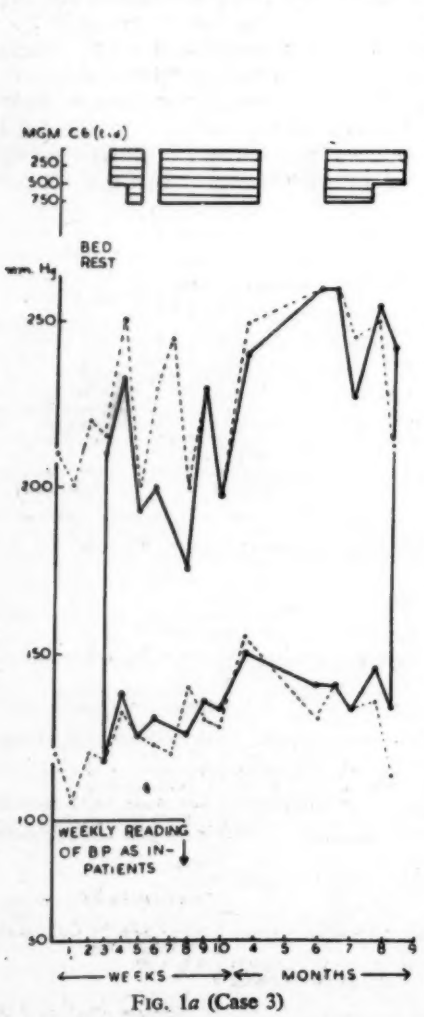

FIG. 1*a* (Case 3)

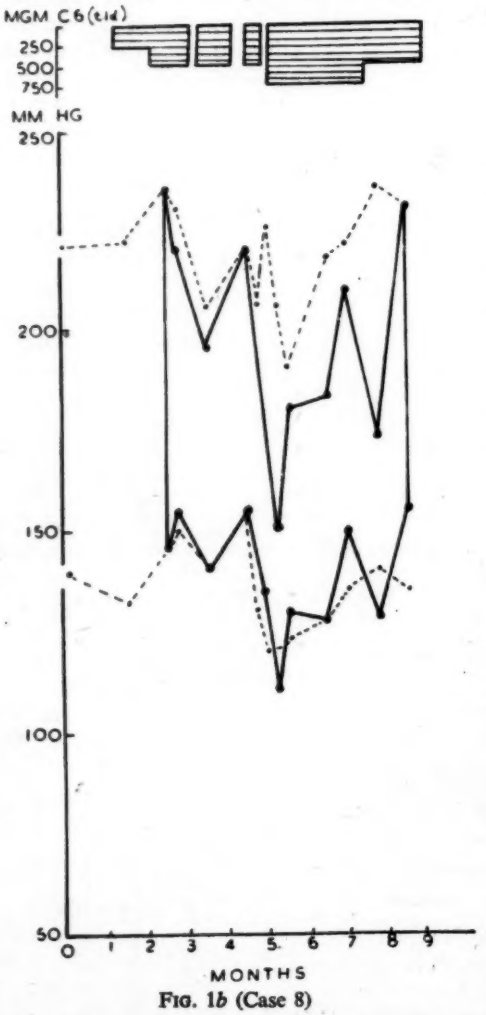

FIG. 1*b* (Case 8)

FIGS. 1*a* and 1*b*.—Showing upright (between solid lines) and recumbent blood pressures taken under relatively standardized conditions at intervals throughout treatment in two cases adjudged as failures on C6 therapy.

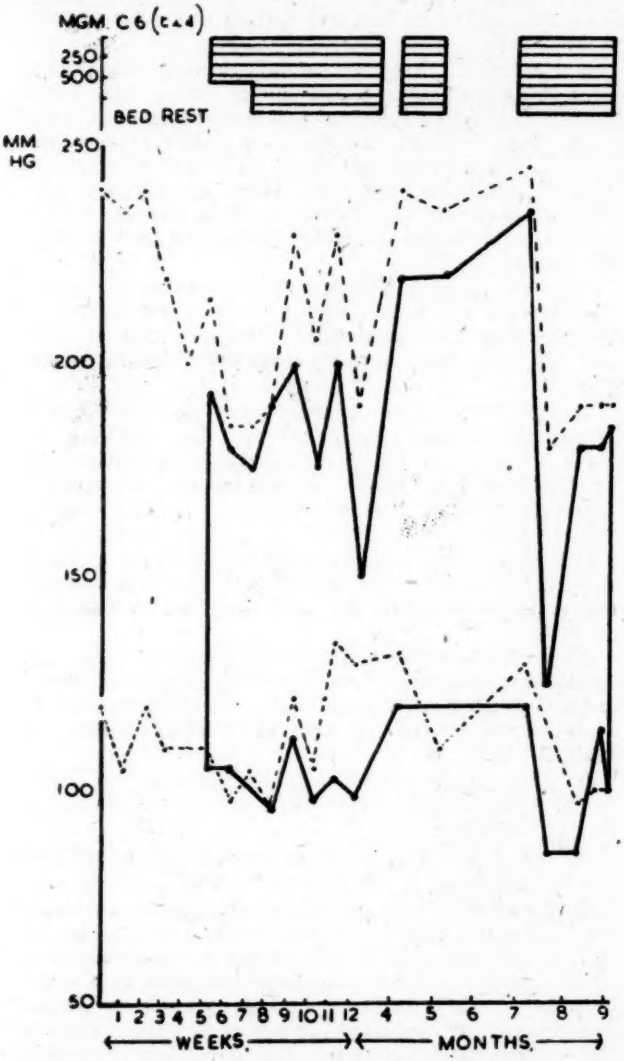

FIG. 2.—Case 5. Showing upright (between solid lines) and recumbent blood pressures taken under relatively standardized conditions at intervals thoughout treatment in a case adjudged to be a success on C6 therapy. The second course of treatment (months 7-9) had a much more pronounced effect on blood pressure than the first

either been negligible or been accompanied by so much disability as to make continuance of effective dosage impracticable. As has been indicated, patients in whom the blood pressure is lowered by methonium therapy manifest, in addition, a certain degree of postural hypotension. Without doubt, as in the post-splanchnicectomy state, this postural hypotension makes its contribution to the clinical improvement of the patient. We have found that the margin between an adequate and an excessive dose is small. Moreover, cases apparently stabilized satisfactorily are liable to suffer from time to time from critical hypotension which may disable them for an entire day. There is reason to believe that the irregularities of therapeutic effect may be associated with variation in absorption of the drug. We have found hypotension to occur, for example, in the presence of constipation or of anorexia.

Headaches

Of our fifteen cases twelve complained of headaches. Of these, eleven were relieved or substantially improved. The failure was Case 15, in which patient drug treatment may have been inadequate. The only useful comment would appear to be that of all the manifestations of hypertension headache is the most easily relieved.

Cardiac Status

We have used this term as a convenient abbreviation. It represents our general assessment of cardiac efficiency as indicated by clinical signs and symptoms, together with radiological and electrocardiographic findings. Of our fifteen cases, nine showed evidence of cardiac damage. We record three of these as improved. All three were relieved of dyspnoea. Before treatment this had been incapacitating and had been a primary reason for admission to hospital. After the establishment of C6 therapy, dyspnoea was relieved and normal activity became possible. In one case there seemed to be diminution of the electrocardiographic signs of left-ventricular preponderance in heart strain and in another the cardio-thoracic ratio showed progressive reduction. In general, the effect of C6 therapy on the severer manifestations of hypertensive cardiac disease has not been striking.

Renal Function

We are not in a position, in respect of the present series of cases, to discuss in detail this aspect of hypertensive disease. In general we have found no striking change in renal function under C6 therapy. We have found, however, that it is possible to lower blood pressure over a period of many months (ten, Case 1 ; seven, Case 9) without deterioration of renal efficiency. In the single case (No. 8) in which renal function has deteriorated, this has been associated with evolution of the malignant phase despite C6 therapy.

Eye Grounds

The changes in the eye grounds in hypertension are of two types: (1) Narrowing, hardening, and tortuosity of the arteries, alteration in A/V ratio. It is unlikely that these changes will be affected by any form of treatment. (2) Exudative phenomena—oedema, haemorrhages, exudates. Theoretically, these may be absorbed if their cause be removed. Of our fifteen cases, five showed exudative phenomena initially. Two (Cases 1 and 9) have shown over a period of many months slow improvement in oedema of retina and nerve heads respectively. One (Case 8) has entered the malignant phase and has developed papilloedema, haemorrhages, and exudates despite treatment. In general, C6 therapy has not produced striking changes in eye grounds. It is, of course, obvious that prolonged study of many cases will be necessary before conclusions can be drawn regarding the degree and duration of hypotension necessary to reverse retinopathy.

Summary and Conclusions

Our study represents a tentative exploration of the possibility of long-term management of essential hypertension by oral administration of drugs. The drug used has been hexamethonium bromide (C6), and for all practical purposes it has been the sole therapeutic weapon employed in the 15 cases presented. These cases have been accepted as they offered, without any attempt at selection. It is our impression that methonium therapy is not subject to the extremely restrictive criteria which govern surgical "treatment" of hypertension. Some of our cases have been under treatment for nearly a year, the majority for more than six months. So far as we have seen, the drug exerts no specifically harmful effects over such periods, and it may well be that indefinitely prolonged treatment will prove tolerable. We agree, of course, with Campbell and Robertson (1950) that the exact place of methonium compounds in the treatment

of hypertension has yet to be defined. Nothing suggestive of "cure" by a course of treatment of limited duration, as described by these authors, has occurred in our series. It may be that our cases have been of more chronic and fixed type. Even in a proportion of these, however, we have found it possible to exercise a useful measure of control.

The advantages of this new method of management of hypertension are obvious. The principal disadvantages appear to be two. First, the daily dosage of the drug necessary to produce a useful effect varies greatly from patient to patient. Secondly, the effective dose is separated from the disabling dose by an increment which is only fractional. Indeed, we have found it impossible in some of our cases to reduce blood pressure without producing disablement.

We feel justified in regarding 5 of our 15 patients as significantly benefited by methonium therapy. In brief, the benefit has consisted in reduction of blood pressure and relief of symptoms. We have no evidence that the unknown underlying lesion has been reversed, or even modified.

Our thanks are due to junior colleagues too numerous to mention individually for much assistance in the recording of blood pressures; to Professor W. J. B. Riddell and his staff for sustained interest in the retinal findings in certain cases treated at the Western Infirmary, Glasgow; and to Professor C. F. W. Illingworth and Dr. E. G. Oastler for facilities and helpful advice freely given. Messrs. May and Baker provided generous supplies of hexamethonium bromide and, in addition, much technical information.

APPENDIX

A Successful Case

This patient (Case 1 of the series), a married woman aged 29, had eclampsia in 1946 during her only pregnancy, which terminated in a stillbirth. High blood pressure and albuminuria have persisted since then. Recently she had headache, palpitation, and dyspnoea. Her mother was hypertensive; her father died young of heart disease.

She was admitted on January 6, 1950, to the medical service of Dr. W. R. Snodgrass. While under treatment for five weeks by rest in bed and sedation her blood pressure was maintained at a very high level, varying between 240/135 and 260/140. On February 10 it was decided to investigate the therapeutic effect of C6 and C5.

Injection intravenously of 22 mg. of C6 produced a sharp hypotensive response, the blood pressure falling from 260/140 to 155/105. The effect was maximal in one hour and passed off slowly over a period of six to nine hours.

Tests carried out on seven consecutive days had roughly comparable results, and attempts were made to achieve continued hypotensive effects by injections given three or four times daily. These met with a varying degree of success, but in general the shape of the blood pressure graph, with its dramatic initial fall and slow rise, indicated that therapeutic success was not to be expected with parenteral administration, which in any case was too inconvenient to be practicable as a long-term policy.

After a day without methonium therapy during which blood pressure rose to its former level, C5 was administered in doses of 22 mg. thrice daily on February 18 and 19. The results achieved were similar in nature to those with C6, but less in degree, and on the morning of February 20 the patient had a hypertensive crisis with violent headache, vomiting, nystagmus, and deafness in the left ear. The blood pressure was unregistrable on the ward equipment, the systolic pressure being in excess of 260 mm. Hg and the diastolic 150 mm. Hg. After an injection of 22 mg. of C6 the pressure fell in two hours to 190/110 mm. Hg and symptoms disappeared, leaving the patient exhausted. It was decided, following this emergency, to persist with C6 rather than C5.

On February 20, in view of the possibility that the hypertensive crisis might indicate the presence of a phaeochromocytoma, a piperoxane test was carried out, with negative result.

On February 22 a scheme of oral therapy with C6 was begun, and continued up to the time of writing. The initial dosage was based on that employed at that time by Kay and Smith (1950) in their work on cases of peptic ulceration, 0.5 g. being administered thrice daily before meals, in capsules, tablets, or solution. There was no significant difference in the results obtained by these different methods of administration, but the tablets proved the least disagreeable to take.

With this dosage it was possible to maintain the patient symptom-free and fully ambulant, with a blood pressure markedly lower than previously. Pressures recumbent averaged 230/130, while those standing were lower, averaging 205/120.

As the course went on there were at times signs of developing tolerance for the drug. For example, the degree of postural hypotension steadily diminished and the blood pressure tended to rise slowly. On June 7, therefore, the dose was raised to 0.75 g. t.i.d. and on June 15 to 1 g. t.i.d.

This dosage was completely effective in controlling the blood pressure, but "side-effects" were disabling, and after two weeks it was clearly necessary to reduce the amount of the drug.

With some difficulty a dose at once effective and tolerable was devised—namely, 1.75 g. daily, 1 g. being given at noon and 0.75 g. at 8 p.m. On this dosage the blood pressure was of the order of 160/100 mm. Hg and side-effects were minimal.

On June 29 C6 therapy was discontinued. The blood pressure rose steadily. On July 2 it was 230/140 and on July 11 260/134.

C6 was restarted at a dosage level of 0.5 g. t.i.d., and was continued up to the time of writing.

On September 14 the patient had difficulty in making her way to hospital, feeling extremely weak, tired, light-headed, shivery, and cold. Her blood pressure was unusually low—145/95 lying and 132/97 standing—and pulse 80 a minute in either position. These findings seemed to indicate development of increased sensitivity to the drug, but the capsules which she was taking at that time were found to contain 0.65 g. of C6 instead of 0.5 g. as intended. She had been taking three of these capsules daily before meals. The dosage was adjusted once more to 0.5 g. t.i.d. The blood pressure rose once more to its former average levels.

On September 28 the blood pressure was found to vary during the period of observation between 250/150 lying and, in the latter part of the day, 175/105 standing.

As we have pointed out, it is extremely difficult to devise a means of registering variations of blood pressure over a period of many months, and if the averages of a considerable number of readings at intervals are taken it may in the end be difficult to establish any general picture of the effect of the drug. In this case, however, such averages taken regularly during the 10 months, throughout which the patient was completely ambulant and performing normal household duties, under treatment with C6 were significantly lower than those constantly obtained during a period of five weeks' rest

Comparison of Status Before and After Treatment

	Before Treatment	After Treatment
Symptoms	Headache, palpitation, dyspnoea	*Nil*, apart from drug effect
Blood pressure ..	240/135 to 260/140	Average lying 220/135 and standing 190/120
Urine	Albuminuria	Albumin disappeared early in course of treatment and has not been recorded since
Fishberg	1000–1014	1002–1012
Blood urea ..	52 mg./100 ml.	50 mg./100 ml.
E.C.G.	Left ventricular preponderance	Left ventricular preponderance less severe

in bed with sedation. The average lying blood pressure was of the order of 220/135 and the standing figure 190/120. The pulse rate remained fairly constantly in the region of 80 a minute whether standing or lying.

Attempts were made to assess renal function on very many occasions during the course of this treatment. In general, the findings of the urea-clearance test were extremely erratic, and the impression is that technical errors were of such magnitude as to render the results worthless. The blood-urea figures were:

January 10	52 mg./100 ml.
„ 31	57 „
February 22	Sustained course of oral C6 begun.
March 4	71 mg./100 ml.
„ 14	61 „
„ 17	52 „
„ 25	54 „
May 19	46 „
June 30	45 „
July 11	50 „
October 6	59 „
November 24	50 „

Lowering of blood pressure was not associated with diminution of renal efficiency.

Ophthalmoscopic Findings

The eye grounds were examined on numerous occasions by Professor W. J. B. Riddell and Dr. R. Leishman. In general, they showed no striking change. Reports at the beginning and the end of the course of treatment are as follows:

February 25.—"The optic disks show fibrous veils of congenital origin. The A/V ratio is 1:2, accounted for by diminution of calibre in the arteries, which are of copper-wire appearance and show marked calibre variation. There is concealment of the veins at A/V crossings. There is no oedema of the disks, but there is oedema of the retina along the course of the main vessels. There are no haemorrhages or exudates and no pigment disturbance. In the left eye, about 2 p.d. above and temporal to the disk, there is an area of collateral vessel formation, probably the result of previous branch thrombosis in a venule. The appearances are those of hypertension in the retinal vessels."

October 7.—"*O.E. Right*: The disk is normal in colour. The physiological depression is present. Fibrous tissues of congenital origin are seen on the disk surface. The disk margins are well seen. The A/V ratio varies between 1:2 and 2:3. The arteries show a colour change. Light reflex is broad and dull. There is well-marked concealment of the veins at A/V crossings. The arteries show calibre variation. There is a slight degree of oedema of the retina along the course of the main vessels. *O.E. Left*: The findings are similar. These appearances suggest hypertension in retinal vessels which are affected by arteriosclerosis. There is no evidence of significant vascular breakdown."

Side-effects

The most constant side-effect was constipation, which gave trouble throughout treatment. On dosage near the upper limit of comfortable tolerance, visual disturbance with failure of accommodation was troublesome. On the heaviest dosage of 3 g. daily the patient was almost incapacitated, with marked weakness and giddiness, especially on rising in the morning. Appetite was poor, and she was troubled with smarting and watering of the eyes and running of the nose. On occasion she was compelled to remain in bed most of the day. In general, however, side-effects were not a serious inconvenience, and for the greater part of the time that she was on oral C6 therapy she was able to do all her own housework in comfort and to travel from the country to hospital once a week to spend a whole day in the wards for continuous observations on blood pressure and pulse rate.

In late September, 1950, the patient began to complain of extreme dryness of the scalp and falling of the hair. At the same time she noticed that she tended to perspire much less than formerly. This disturbance of the hair and scalp responded to simple measures. It may or may not have been a direct result of methonium therapy.

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A CLINICAL STUDY OF THE EARLY POST-GASTRECTOMY SYNDROME

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The description of the syndrome which follows is based on the records of cases studied in a follow-up clinic at Bristol Royal Infirmary and Southmead Hospital, Bristol.

When the routine study of post-gastrectomy cases was begun it was soon obvious that patients who exhibited symptoms after meals fell into two major groups, as described by Adlersberg and Hammerschlag (1947). These were as follows:

Group 1.—Cases in which symptoms occurred towards the end of a meal or within a few minutes of its completion. This group corresponds to the "dumping syndrome" of most authors, but we prefer the term "early or immediate post-gastrectomy syndrome."

Group 2.—Cases in which the symptoms occurred during the second or third hours after meals—to be referred to as the "late or delayed post-gastrectomy syndrome."

Early or Immediate Post-gastrectomy Syndrome

This variety of the post-gastrectomy syndrome is rather more common than the delayed type. It occurred in 79 of the 660 cases reviewed (11.97%). In our opinion it constitutes the major problem, as it accounts for the most severe cases. Typically, there is quite a sudden onset, the patient often "bracing himself up" in his chair as the syndrome starts. There is a feeling of fullness and distension in the epigastrium, associated with nausea and lassitude. Vomiting is rare, but should it occur it affords considerable relief, the patient often going on to resume and enjoy a full meal. The epigastric sensation is sometimes described as "painful," and may radiate to the back. The onset of the abdominal symptoms is associated with a spreading sense of warmth or cold, and accompanied by perspiration, as a rule most marked on forehead and face. There is usually definite pallor, and frequently a "goose-flesh" appearance of the skin. The patient complains of palpitations and occasional throbbing in the head and neck, and often expresses a desire "to get to an open window or out

into the fresh air." Some patients experience borborygmi and have diarrhoea, whilst others have eructations. Initially the onset of these symptoms causes the patient marked apprehension, but this becomes less evident as the attacks are repeated.

On the average, the attack lasts from 30 to 45 minutes. A rise of pulse rate and of blood pressure accompanies the symptoms. In no case was there a profound hypotension as noted by Perman (1947). With regard to the relationship of the symptoms to coincident changes in the blood-sugar level, it was repeatedly observed that this early syndrome occurred whilst the blood sugar was rising to its peak.

TABLE I.—*Relative Frequency of Symptoms and Signs in 79 Cases of Early Syndrome*

Epigastric fullness and distress	79
Pallor	76
Failure to gain weight	73
Sensation of warmth and sweating	72
Nausea	64
Palpitations	50
Vomitus of bile-stained fluid	41
Diarrhoea	10
Eructations	9
Borborygmi	8
Vomiting of food	5
Sensation of cold	3

All the patients noted that the symptoms started very soon after the operation, usually before leaving hospital, when they began to take solid food again. The late onset noted by some authors may be accounted for by the delayed resumption of normal feeding following operation.

Of the 79 patients, 71 noted that their attacks usually occurred after the heaviest meal of the day. "It occurs after a cooked dinner" was a frequent response. Most patients co-operated well in recording their attacks, and it was evident that no particular foodstuff was culpable; it was the bulk of the meal that constituted the chief factor in precipitating an attack. So true is this that patients know exactly how much they can eat with safety. They know that "the extra slice of bread" or the "extra spoonful of food" will cause an attack. The addition of a drink, especially a hot drink, at the end of a meal also often precipitates the syndrome. It is probable that these voluntary restrictions of food intake on the part of the patient account for the persistent failure to gain weight after the operation. The very nature of the condition precludes taking more food, in contradistinction to the late syndrome, in which marked relief occurs if more food is taken.

Of the 79 patients, 41 (51.8%) complained of vomiting a bile-stained fluid after meals. This type of vomiting may occur independently of the early post-gastrectomy syndrome, but when it occurs with it it has an interesting relationship. The vomiting is usually precipitated by changes of posture, especially stooping down, and it occurs about 30–40 minutes after meals. It does not happen every day, but two or three times weekly, or perhaps once every three weeks or so. The attacks usually decrease in frequency and completely disappear within one to two years of operation. The occurrence of bile vomiting with the early syndrome is usually associated with considerable relief, and the patient can take much larger meals without ill effect. After a few days the patient finds that smaller and smaller meals cause symptoms, and this goes on until the next vomiting attack, which again brings relief. This often gives the early syndrome a cyclical character.

It must be stressed that it is the combination of abdominal symptoms and vasomotor phenomena that constitutes the syndrome. Virtually every patient who has had a gastrectomy performed gets a sensation of fullness in the epigastrium after meals, but only a minority have associated vasomotor features.

The area to which the abdominal sensations are referred is worthy of notice. Nearly all post-gastrectomy patients refer the feeling of distension to the periumbilical area (Fig. 1, A). Cases presenting the syndrome, however, refer the sensation first to a position high up in the costal angle (Fig. 1, B1), then more generally to the epigastrium (Fig. 1, B2).

Most patients showing the early syndrome state that lying down affords them considerable relief, and they may occasionally fall asleep. We have been very impressed by this, and by the clinical fact that some patients have to lie down to take their meals.

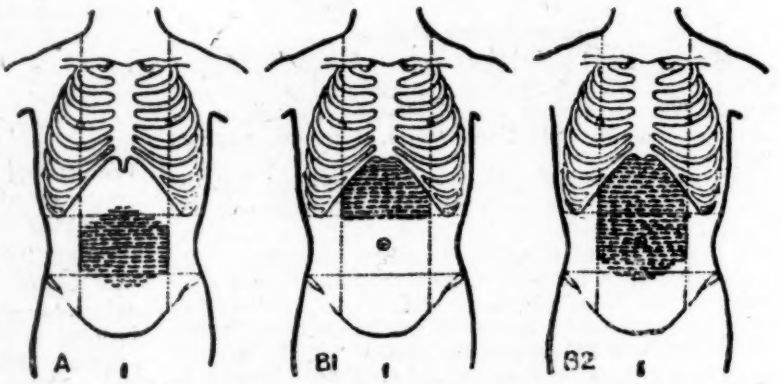

FIG. 1.—A: Indicating site of reference of sensation of fullness in most cases of gastrectomy not exhibiting the early post-cibal syndrome. This is the area of reference of fullness in the tests with jejunal distension. B1: Indicating the initial site of reference of the sensation of fullness in cases with the early post-cibal syndrome. This is the area of reference of fullness when a mercury-loaded bag is in the gastric remnant. B2: Indicating the spread of the area of reference of the sensation of fullness in cases with the early post-cibal syndrome—i.e., a summation of A and B1.

Duration of the Syndrome after Operation

In this series of 79 patients, 18 had recovered by the time the investigation was carried out, whilst the remaining 61 (77.2%) had persistent symptoms for 2 to 11 years. This observation seems to be contrary to the generally accepted view that the condition usually disappears in one to two years. This long duration of the early syndrome has been noted by two authors only: Custer *et al.* (1946) considered that all but the mildest of cases lasted indefinitely; and Smith and Jordan (1948) observed that this syndrome persisted for more than five years in 50% of their cases.

Perhaps the most interesting observation in this series is that all the symptoms do not disappear at the same rate. The sensation of fullness invariably disappears first, the vasomotor phenomena persisting for several years afterwards. In the 18 cases in which the syndrome had disappeared, the epigastric fullness had ceased by the end of the second year after operation in 11, whilst in 7 it persisted until three years had elapsed. In every case the vasomotor features continued for a further period varying from two to four years.

Severity of the Syndrome

In any review it is very difficult to assess degrees of severity. In this series the simplest possible classification of severity has been adopted, and the cases are divided into two groups as follows: (1) severity sufficient to cause economic loss to the patient; and (2) symptoms present, but the patient able to follow his occupation.

It was found that 31 of the 79 cases were severe enough to cause periodic loss of work, whilst the remainder could manage their daily occupation. These 31 cases represent 4.7% of the 660 cases reviewed. Table II shows a comparison of groups presented by various authors.

TABLE II.—*Comparison of Groups of Mild and Severe Cases of Early Syndrome*

	Present Series	Tanner (1948)	Custer *et al.* (1946)
Total No. of gastrectomy cases	660	91	500
No. of cases with early syndrome	79 (11·97%)	26 (28·5%)	28 (5·6%)
Severe cases	31 (4·7%)	7 (7·6%)	16 (3·2%)
Mild cases	48 (7·27%)	19 (20·8%)	12 (2·4%)

We are confining our attention here to the early syndrome and leaving the clinical details of the delayed syndrome for discussion in a later article. In order to clarify the clinical differences between them, however, we include a comparative summary of the essential clinical features of the early and delayed post-gastrectomy syndromes (Table III).

TABLE III.—*Comparative Summary of Essential Features of Early and Delayed Post-gastrectomy Syndromes*

	Early Syndrome	Delayed Syndrome
Incidence	12%	5·15%
Relation to meals	Immediately after meal	During second or third hour after meal
Duration of attack	30–40 minutes	30–40 minutes
Long-term duration	Severe cases indefinitely	2–5 years
Relief by	Rest by lying down	More food
Aggravated by	More food	Exercise
Chief precipitating factor	Bulk of meal	Carbohydrate content of food
Chief symptoms	Epigastric fullness; sweating; sensation of warmth; tachycardia	Tremor; giddiness; epigastric emptiness; nausea
Probable nature	Mechanical	Hypoglycaemic

General Statistical Review

Our study of this subject was started in 1947 and has continued to the present time. In addition to the determination of the incidence of post-gastrectomy symptoms after gastrectomy in general, a major point in the investigation was to ascertain if there was any variation in the incidence following the different types of operation in common practice. For this purpose a series of patients surviving consecutive operations of partial gastrectomy was collected. Owing to the kindness of our colleagues, 660 cases were available for study, all having been in the Bristol Royal Infirmary, the Bristol General Hospital, or Southmead Hospital during the 17-year period 1933–49. The criteria of selection were simple: (*a*) the operation was performed for benign peptic ulcer; (*b*) adequate operation notes were necessary; (*c*) the patients lived within a short distance of Bristol, so that follow-up was possible. Table IV shows the incidence of both the early and the delayed syndrome following the various types of gastrectomy practised in this centre.

TABLE IV.—*Analysis of Cases*

Type of Operation	No.	Early Syndrome	Delayed Syndrome
A. Billroth I	102	0	5 (4·9%)
B. Polya–antecolic without valve	109	15 (13·7%)	6 (5·5%)
C. Polya–antecolic with valve	168	27 (15·7%)	8 (4·7%)
D. Polya–retrocolic without valve	104	14 (15·6%)	6 (5·7%)
E. Polya–retrocolic with valve	57	8 (14%)	3 (5·2%)
F. Polya–Moynihan	120	15 (12·5%)	6 (5%)
Total	660	79 (11·97%)	34 (5·2%)

In this table, the subgroups B to E denote operations in which the anastomoses were antiperistaltic in type. Type B was the procedure usually referred to as the Balfour operation, but which was first performed by Kroenlein in 1888, in which the stoma was the full width of the end-to-side gastro-jejunal anastomosis. Type C, a modification of B, incorporated a valvular anastomosis of the "Hofmeister–Lake" type to restrict the size of the stoma. In this series, the stoma was large enough to admit two fingers. Type D was really the original Polya–Reichel–Bergmann operation, in which a retrocolic gastro-jejunal anastomosis was made. Type E represented the Finsterer modification of D, incorporating a valvular anastomosis again. Type F, the Moynihan modification of the Polya operation, was antecolic but with an isoperistaltic anastomosis.

Further analysis showed that the site of the ulcer—that is, duodenal or gastric—and the age and sex of the patient did not affect the incidence of the syndrome.

The important factors which emanate from this analysis, therefore, are as follows: (1) the incidence of the early post-gastrectomy syndrome is 11.97%; (2) the incidence of the delayed syndrome is 5.2%; (3) the early syndrome does not occur after the Billroth I operation, but does occur after any modification of the Polya operation; the particular modification does not affect the incidence; and (4) the delayed syndrome occurs with equal incidence after any type of gastrectomy.

Effect of Posture

Observations were made on these patients during the time they consumed the main meal of the day—that is, the meal which caused symptoms most frequently. In hospital it was the midday meal which was responsible and therefore observed. The effect of posture was studied in the following ways:

1. Lying Down Immediately After the Onset of Symptoms

Each of the 61 patients studied in hospital was observed on three or four occasions while he ate his heaviest meal. When the syndrome occurred he was instructed to lie down immediately and the effects were observed. In 54 (89%) of the 61 cases the effect of this change of posture was very marked, and may be described as follows: (*a*) The vasomotor symptoms, the tachycardia, the pallor, and the feeling of warmth and sweating disappeared first, all within five minutes. (*b*) The sensation of fullness, initially spread over the upper abdomen, disappeared more slowly, taking 10–15 minutes. The fullness in the subcostal angle disappeared first, but the similar sensation around the umbilicus persisted longer. (*c*) The duration of the whole syndrome was thus reduced from 30–45 minutes to 10–15 minutes.

In the remaining seven cases, although the symptoms were reduced in intensity, the duration was reduced only very slightly, by about five minutes.

2. Effect of Taking Meals Lying Down

This particular test was applied on three or four occasions to each of the 61 cases. The effect of this position was noted only while the main meal of the day was being eaten. In 41 cases (67%) the patient complained of fullness referred to the umbilicus, while the remainder were symptom-free. In two patients who complained of fullness there was coincident tachycardia and sweating lasting for 5–10 minutes.

3. Effect of Lying Down Before a Meal

The 61 patients under observation were instructed to lie down for a period of half an hour before the main meal.

The meal itself was eaten with the patient sitting up. In 49 (80%) the syndrome did not occur. They had mild transient fullness around the umbilicus, but no other symptoms. In addition they could consume 3–9 oz. (85–255 g.) more food without ill effect. In the remaining 12 cases the syndrome occurred with its normal intensity. During the period prior to the meal when the patients were supine, nine vomited clear bile-stained fluid in amounts varying from 9 to 15 oz. (255–425 ml.).

In order to clarify this interesting observation the tests were repeated with a Ryle's tube in position while the patients were lying down. It was noted that in the erect position

TABLE V

No. of Cases	Amount of "Bile" Aspirated
8	16–23 oz. (454–653 ml.)
39	10–15 oz. (284–425 ml.)
14	6–9 oz. (170–255 ml.)

either no "bile" at all or only about 1 oz. (28 ml.) could be aspirated via the stomach tube. During the period of lying down, however, large amounts of bile-stained fluid could be aspirated with ease, the amounts being shown in Table V. This indicates that if the afferent loop can be emptied before a meal the chances of the early syndrome occurring are very much reduced and a much larger meal can be taken in consequence. In the erect position, the afferent loop loaded

FIG. 2.—Illustration of kinking of the afferent loop of the anastomosis at its upper angle.

with bile and pancreatic secretions tends to be kinked at its upper angle, where it joins the lesser curvature of the stomach in antiperistaltic anastomoses (Fig. 2). This impedes free emptying of the afferent loop. At a second operation after gastrectomy the afferent loop can usually be distinguished from the efferent loop, the former being dilated and hypertrophied, no doubt owing to its difficulty in emptying. Occasionally we have found it is the efferent loop which is dilated, especially when there is a short loop with a retrocolic anastomosis. When the patient lies down the kinking effect is reduced and the afferent loop can empty itself more readily. In other words, it seems that the actual weight of the afferent loop is a factor in producing the early syndrome. If it is full and therefore heavy, the syndrome readily occurs; whereas if the loop is emptied and its weight reduced the syndrome is far less likely to occur. This explains the finding that patients with retrocolic short afferent-loop anastomoses can eat larger meals before symptoms occur as compared with patients with long-loop antecolic anastomoses.

As a result of these studies the following conclusions may be deduced: (1) Change from the erect to the supine position readily relieves the early post-gastrectomy syndrome, the vasomotor component of this syndrome being more readily and speedily relieved than the abdominal counterpart. (2) In the erect position, kinking of the afferent loop of an antiperistaltic gastro-jejunal anastomosis readily occurs, rendering emptying difficult. This causes periodic retention of its contents, which is an important factor in the causation of both the early post-gastrectomy syndrome and the "bile" vomiting. If the afferent loop is emptied the early syndrome does not occur so readily.

Incidence after Gastro-enterostomy

During the performance of these tests it became evident that rapid emptying of the stomach was not the major factor in the causation of the syndrome. It was accordingly decided to review a series of cases in which simple short circuit had been performed, without gastric resection—that is, simple gastro-enterostomy. This operation is not often performed here, and only 73 cases were readily obtained for study. Clinically, 19 cases (26%) noted fullness after meals, again referred to the central abdomen. Only in two cases (2.7%) did patients note nausea, sweating, palpitations, and a sensation of warmth immediately after meals. Radiological examination showed that in 51 cases (69.8%) the emptying time was within 80 minutes, the remainder within two hours.

It therefore seems that the early syndrome is very rare after simple gastro-enterostomy, and this finding has been confirmed by Avery Jones (1948, personal communication).

Discussion

The results of these clinical and experimental studies (see Butler and Capper, 1951) permit the following deductions:

1. The syndrome did not occur after 102 consecutive cases of the Billroth I operation. This finding has been confirmed by personal communication in 1949 with Professor Grey Turner, and with Dr. J. M. Waugh, of the Mayo Clinic, where a Billroth I procedure is done whenever possible for this very reason. Further, Perman (1947) advocates conversion of Polya gastro-jejunal anastomoses to the Billroth I type as the treatment of the "dumping syndrome."

2. The syndrome is very rare after simple gastro-enterostomy.

3. The syndrome occurs with equal incidence after all forms of the Polya operation, whether antecolic or retrocolic, antiperistaltic or isoperistaltic, and whether or not there is an anastomosis of a valvular type. The syndrome occurs, however, with smaller meals in antecolic anastomoses compared with retrocolic anastomoses.

4. Jejunal distension tests give rise to a sensation of fullness referred to the umbilicus, and it is very rare for jejunal distension to cause vasomotor upset. Further, there seems to be no difference in the sensitivity of the jejunum between cases with the syndrome and those without it.

5. Change from the erect to the supine position greatly relieves the syndrome, the upper abdominal sensation of

fullness and nausea together with the vasomotor features disappearing first, the central abdominal fullness disappearing later.

6. Cases of gastrectomy with the syndrome have fullness high in the costal angle after meals, the sensation spreading to the whole of the upper abdomen afterwards. Cases of gastrectomy without the syndrome, but with fullness after meals, usually refer this sensation to the umbilical area.

7. If and when the syndrome disappears completely all the symptoms do not go at the same rate. The central abdominal sensation of fullness disappears first, followed several months or years later by the vasomotor symptoms.

8. Both clinically and experimentally, the chief factor in causing the syndrome, especially the upper abdominal heaviness, the nausea, and the vasomotor features, appears to be the weight of the meal, and the syndrome can be reproduced experimentally by inert factors such as barium emulsion and a mercury-loaded bag in the gastric remnant (Butler and Capper, 1951).

9. Emptying of the afferent loop greatly reduces the incidence of the syndrome. Further, experiments indicate that the state of the afferent loop and the weight of the meal are complementary. If the loop is relatively empty or short a heavier meal can be taken than when the loop is full and distended. It is felt that the weight of the afferent loop is an important feature in its relation to the weight of the meal.

Prevention

If the major factor causing this syndrome is traction on the gastric remnant by a heavy afferent loop, plus the weight of food, then it should be possible to prevent the syndrome occurring by ensuring adequate support for the stomach at operation. In addition to reconstructing peritoneal supports for the stomach, it is necessary to arrange the anastomosis so that the weight of the heavy afferent loop is not borne by the stomach, because, as has already been shown, the loaded afferent loop is a contributory factor in causing traction.

With the above aims in view, a series of operations was begun in March, 1948, in which a serious attempt was made in each case to correct the factors mentioned. This was done in the following ways:

1. *Support of the Gastric Remnant.*—During the operation a stout silk ligature (or double-thickness linen thread) was passed around the left gastric artery at its highest point on the lesser curvature of the stomach. The ligature was firmly tied so that it included the stout thickened peritoneum of the left extremity of the lesser omentum

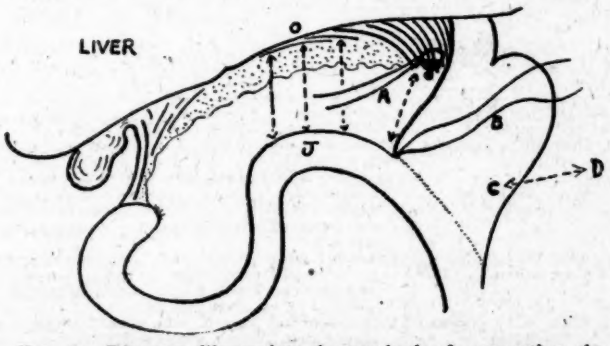

FIG. 3.—Diagram illustrating the method of supporting the gastric remnant: A=The higher of two ligatures on the left gastric artery, passing through the strong peritoneal support of the stomach. B=A long suture at the highest point of the anastomosis. A and B are tied together, thus giving the gastro-jejunal junction full support. The afferent loop J is sutured to the highest part of the gastro-hepatic omentum, which is usually thickened. Below this the lesser omentum is very thin—and is shown dotted. The greater curvature at C can be reattached to the gastro-splenic ligament. Although not a major support, this reattachment prevents rotation of the gastric remnant and the jejunum.

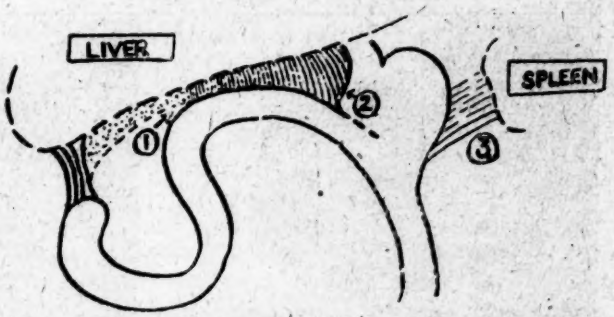

FIG. 4.—Illustrating reconstruction of supports to the gastric remnant. (1) Afferent loop supported by suturing it to upper edge of the lesser omentum. (2) Attachment of upper angle of anastomosis to point of ligation of left gastric vessels. This is the most important support. (3) Greater curvature supported by reattachment of gastro-splenic ligament.

in addition to the artery. The ends of the ligature were left long (ligature A in Fig. 3). The left gastric artery was divided between ligatures below this level for the resection. Later, on completing the anastomosis, a similar double-thickness thread suture was introduced at the upper angle of the anastomosis (ligature B). These two ligatures were then tied together, so that the upper end of the anastomosis was anchored to strong peritoneum as illustrated in Fig. 4. In addition, the gastrosplenic ligament was reattached to the greater curvature of the gastric remnant.

2. *Support for the Afferent Loop.*—This was sutured at three or four points, as shown in Figs. 3 and 4, to the thick rim of peritoneum at the upper edge of the lesser omentum. In this way the afferent loop was slung under the liver and its weight taken off the stomach remnant. The operation performed in each case was an antecolic antiperistaltic Polya operation with a Hofmeister–Lake valvular anastomosis. To date, 128 of these have been performed. A series of 113 of our own cases of the same type was also available, but in this series no attempt at reconstruction has been made.

TABLE VI

		No.	Early Syndrome Cases
Series 1	Polya–Hofmeister. No gastric or afferent loop supports ..	113	15 (13·2%)
Series 2	Polya–Hofmeister with reconstruction of supports ..	128	1 (plus 1 doubtful) (1·5%)

Table VI shows the results in these two series. In series 1 the incidence of the early syndrome was 13.2% (15 cases out of 113), whilst in series 2, in which reconstruction had been carried out, there was a marked reduction in the incidence of the early syndrome to 1.5% (1, and 1 doubtful, out of 128).

The difference in the incidence is significant. The case mentioned in series 2 was a very definite instance of the early syndrome. *X*-ray films showed considerable descent of the stoma, and it was therefore assumed that the reconstruction at operation had been inadequate. With reference to the doubtful case it was very difficult to decide whether it was a true case or a functional disorder; the patient had many symptoms but no signs except marked afferent-loop reflux. The post-operative *x*-ray follow-up of the cases in series 2, however, confirmed that descent of the stoma was reduced after reconstruction of anatomical supports of the stomach. Fig. 5 illustrates this fact.

Surgical Treatment of Early Post-gastrectomy Syndrome

As a result of the information obtained from the preceding investigations it was considered worth while to advise surgical intervention in those cases in which severe

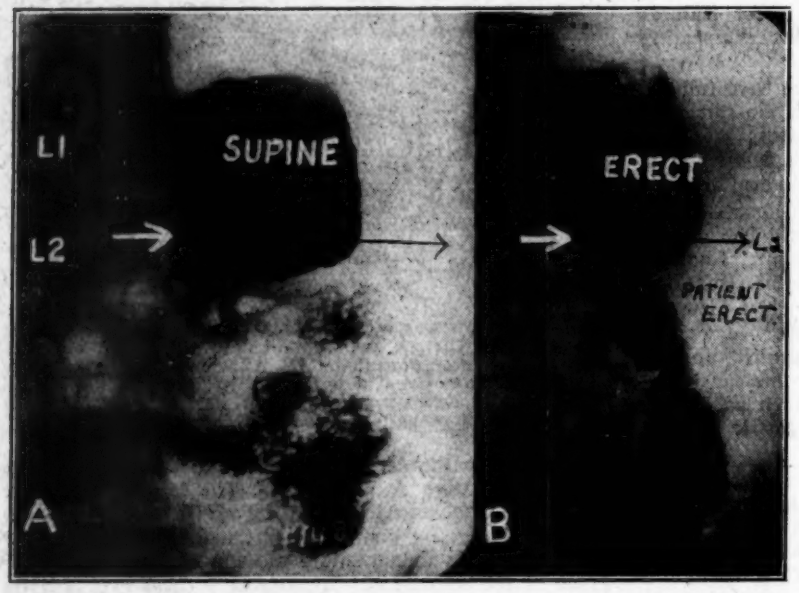

FIG. 5.—Illustration of control of stretch of the stomach remnant by adequate support; there is no descent when the patient changes from supine to the erect position.

and crippling disability existed. Only cases in which the syndrome was reproduced by the mercury-loaded bag were operated upon, and to date eight such cases have been treated by surgery. The steps of the operation were essentially those already described in the prevention of the syndrome, and are briefly as follows:

The abdomen is opened through a midline or upper left paramedian incision. There is usually a moderate amount of filmy or even thick adhesions between the anterior surface of the stomach and the liver. At first it may be thought that these would give the required support to the stomach, but on dividing them it is obvious that the lesser curve is all the time hanging almost vertically from the cardia, the stomach being rotated to the left. After the adhesions have been divided the mass of tissue around the left gastric vessels is isolated and ligated by a strong piece of thread, leaving the ends long. The remains of the lesser omentum are then displayed, and especially the thickened fringe of the omentum which lies immediately under the liver. This will give a firm bite for sutures to act as a support to the lesser curve. A series of thread sutures are then put in every 0.5 cm. between the lesser curve and its supporting structures—that is, first of all the right crus of the diaphragm and from there to this thickened edge of lesser omentum. These are tied in order, and finally the upper angle of the anastomosis is brought up to the stitch which was left long around the left gastric vessel. From this point the afferent loop of the jejunum (in the antecolic Polya operation) is supported by stitching it similarly to the right half of the remaining lesser omentum until the fascia over the common bile duct is reached. By this means there is adequate support both for the lesser curve of the stomach and for the afferent loop of jejunum.

It is wise to keep the patient lying flat for fourteen days. The post-operative course is usually without incident, and the patient should be encouraged to eat a full three-course meal between the fourteenth and twenty-first days. It is refreshing to see the change in outlook towards food that rapidly develops, and very soon the patient can take large heavy meals with confidence.

The results are presented in Table VII. Of the eight cases treated seven have been cured.

Summary and Conclusions

Investigations have been made into the causation of the early post-gastrectomy syndrome, and as a result the following conclusions are drawn:

1. All the symptoms constituting the syndrome are not due to the same cause.

2. The sensation of fullness after meals referred to the umbilicus, both in cases with the syndrome and in post-gastrectomy cases in general, is due to rapid emptying of the stomach, with jejunal distension.

3. The remaining symptoms that constitute the early post-gastrectomy syndrome—that is, the severe symptoms—are due to traction on the gastric remnant, such traction being due partly to the weight of the meal, and partly to

TABLE VII.—*Results of Operations for Treatment of Early Post-cibal Syndrome (8 Cases: 7 Successes, 1 Failure)*

Case No.	Age and Sex	Original Operation	Pre-operative Test with Mercury-loaded Bag. Amount of Mercury Producing Syndrome	Operation for Relief of Syndrome	Post-operative Mercury Test	Remarks
1	58 M	Polya–Hofmeister for G.U. 18/7/49	7 oz. (198 g.)	31/10/49	15 oz. (425 g.) without symptoms	Excellent result. Patient able to eat as large a meal as he desires. Weight increasing rapidly
2	40 F	Balfour for D.U. April, 1948	8 oz. (227 g.)	30/11/49	17 oz. (482 g.) without symptoms	Absolutely symptom-free. Very pleased with result; can now eat any size meal without difficulty. Gaining weight at rate of 3 lb. (0·0 kg.) weekly
3	40 M	Balfour for D.U. January, 1949	8 oz. (227 g.)	15/12/49	16 oz. (454 g.) without symptoms	Unsatisfactory. Although patient could take larger meals, he complained of symptoms two hours later, associated with hypoglycaemia. Regarded as a failure
4	49 M	Polya–Hofmeister for D.U. 1939	6 oz. (170 g.)	10/1/50	16 oz. (454 g.) without symptoms	Excellent; patient well pleased. No symptoms since operation for syndrome. Can eat whatever he likes, as much as he likes. Increased weight by 1 st. (6·3 kg.) in three months
5	52 M	Polya–Finsterer for G.U. 1947	9 oz. (255 g.)	4/2/50	15 oz. (425 g.) without symptoms	Patient very well pleased. Can take full meals much larger than before, and symptom-free, since operation for syndrome
6	50 F	Balfour for G.U. 1947	6 oz. (170 g.)	17/2/50	17 oz. (482 g.) without symptoms	Excellent; symptom-free and increasing in weight
7	46 M	Polya–Finsterer for D.U. 1946	9 oz. (255 g.)	26/2/50	16 oz. (454 g.) without symptoms	Although retrocolic anastomosis—afferent loop still long. No vasomotor symptoms since operation for syndrome, but occasionally central abdominal fullness, though much less. Patient very pleased; is putting on weight, and is now back at his original work as engine driver
8	51 F	Polya–Hofmeister for G.U. 1947	7 oz. (198 g.)	3/3/50	17 oz. (482 g.) without symptoms	Very good result; patient highly pleased. Now symptom-free

the weight of the afferent loop suspended on the gastric remnant.

4. The early post-gastrectomy syndrome can be prevented by suitable reconstruction of anatomical support for the stomach and the anastomosis.

5. In cases in which the syndrome is severe, surgical intervention is worth while and is curative.

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PHAGE-TYPING AND EPIDEMIOLOGY OF SHIGELLA DYSENTERIAE SONNE

BY

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Sonne dysentery continues sporadically, with epidemic outbursts, in this country, and is a recurring nuisance in mental homes, hospitals, and other institutions. The hardiness of the organism when excreted leads to its persistence in unexpected situations. Green and MacLeod (1943) recorded its survival for longer periods than *Bact. coli* in a chlorinated water, and Hutchinson (1947) isolated it from utensils washed in hotel kitchens. The large numbers of ambulant cases with very mild symptoms in any outbreak result in the existence of many unrecognized sources of infection in the community. With this disease, therefore, it becomes more important than in the more severe enteric infections to be able to trace individual strains of organisms from patient to patient, and to identify a particular infection as originating from one particular source among a number of possible alternatives.

Serological methods—so useful in the Salmonella group—are unable to distinguish different strains of Sonne dysentery, and biochemical methods have offered little further success. The phage-typing of Sonne strains, however, by Hammarström (1947), in Sweden, was claimed to have achieved this differentiation. We had found the phage-typing of typhoid strains of considerable use in a Bristol outbreak (Cooper, 1950) because of the number of different types capable of identification (Felix and Pitt, 1934), though the phage-typing of paratyphoid B strains in 1941 (Davies *et al.*, 1942) was of no assistance owing to the widespread incidence of the strain concerned. One of us had previously compared the serological typing of *Ps. pyocyanea* (Mayr-Harting, 1948) with the method of phage-typing (Mayr-Harting, 1949), and it was felt that in Bristol we were in a particularly favourable position to examine the possibility of using Hammarström's phage-types for epidemiological purposes. Hammarström very kindly sent us his type strains and type phages.

Experimental Results

The following is a preliminary report on seven months of phage-typing, with these phages, on strains of Sonne dysentery isolated in Bristol. Even in this brief survey we hope to show that (*a*) new infections occurring during the whole of this period in certain blocks of a mental home, well isolated from the introduction of outside infection, were all of one type; (*b*) that an outbreak in a hospital due to one type was completely cleared up, but the introduction of a patient with a different type at a later date resulted in a new outbreak of this new type; and (*c*) that sporadic apparently unconnected cases in the city often yielded still further types of infection.

The types found and their distribution were as follows:

Type	No. of Strains	Type	No. of Strains
3	30	17a	1
81	13	Coleman	1
66	2	Powell	1
82	2		50

Types 81 and 82 had so far not been isolated in Sweden and have been given their numbers by Dr. Hammarström. The types "Coleman" and "Powell" have not yet been compared with the Swedish types.

Early Outbreak

We found a very marked difference in the distribution of types before and after the summer holidays. All strains of type 81 were isolated early in summer. Four of them were from people unconnected except in so far as they all lived in the more crowded eastern districts of the city. One of these patients was transferred to hospital, and within a few days there was an outbreak in another ward of this hospital involving about a dozen people. A member of this staff has subsequently given a history suggestive of infection, and, though no proof has been obtained of the method of transfer, no other strain of this type has been isolated since early summer except the nine cases typed at that time.

Isolated Infections

After the summer holidays *five* other types were found in the city which had not been isolated in the few months preceding the holidays.

(1) *Type 66* was isolated from a young man who fell ill with dysentery the day after his return from a cycling tour through France. A few months later the same strain in mixed infection with paratyphoid B was isolated from a little girl. The source of both infections in this child is rather obscure, but one factor deserves consideration: the diet of the household included large quantities of mussels and other shellfish.

(2) *Strain 17a* was isolated from a girl and probably was imported from Weymouth. Some time before the onset of the girl's illness her mother fell ill with diarrhoea after a visit to Weymouth, and from then onwards there was a chain of infections of gastro-enteritis in the family. Dr. Hammarström informs us that he has not isolated this type in Sweden, but that he has obtained a strain of this type from Czechoslovakia.

(3) The two strains of type 82 were isolated from a little boy and his father. This family had not been outside the Bristol district for weeks.

(4) and (5). The Coleman and Powell strains were both isolated from students in a teachers' training college, and were of different types. But the movements of the students concerned and the time-table of their illness allow the possibility that their cases are not connected

epidemiologically. Mr. Coleman probably acquired his infection at the college, which had a history of earlier cases of diarrhoea. In the case of Mr. Powell there is very strong support for the assumption that his infection was acquired at his home, where his brother fell ill on the same day, a few days after Mr. Powell returned to college.

Outbreak II

Twenty-three of the 30 cases from May to December due to type 3 have been found in a colony for mentally defective people at intervals over the whole period of this investigation. No other type has been isolated from this colony, and it is a fair assumption that all these infections have been acquired at the colony. By the nature of living conditions and habits of the mentally defective it will be very difficult to do more than confine the outbreak to the particular blocks affected.

Previous records showed that there had been a severe outbreak of Sonne dysentery at a babies' home, involving almost all the babies and staff. One strain of that outbreak had been kept, and was also found to belong to type 3.

Outbreak III

Type 3 was also responsible for an outbreak in the hospital which had suffered earlier in the year from type 81. On this occasion, however, a patient was admitted into the ward with infection due to this type, and the other three cases in this ward were close contacts and obviously infected by him. One other case in another ward had positive cultures of this type on admission.

So far 29 cases of type 3 have been accounted for; the remaining one was an isolated case in the city.

Conclusions

From the foregoing, although the number of strains typed is very small, some conclusions about the kind of information that Sonne phage-typing will yield may be drawn already. The types are very numerous and the isolation of seven different types in a town of moderate size like Bristol during seven months shows that the epidemiological unit is very much smaller than the town. It is indeed very small in space—family or institution—and also seems to be of short duration, unless the circumstances are exceptional, as amongst the mentally defective.

The multiplicity of types and the smallness of the epidemiological unit will make it possible to trace some of the strands in the tangle of the pathways of infection. We hope to obtain strains from outside Bristol and from other parts of the country, to follow in detail such phenomena as, for instance, the appearance of new types after the holidays.

Much remains to be done to establish the degree of stability of the types *in vivo* and *in vitro*. Many technical difficulties, which may occasionally upset the type determination, must have their importance assessed. The influence of the composition of the medium on the phage titre makes some difficulties in correlating results obtained in Bristol and in Sweden. The occurrence of phage-carrying and lysogenic strains may confuse the appearances unless care is taken to avoid these organisms for the propagation and standardization of the phages used. Many of these difficulties have been described by Hammarström in very clear detail, and it seems likely that they do not destroy the main epidemiological importance of type determination on most occasions. Whether examination over a longer period will give rise to important exceptions to the belief that type identity is the result of recent close genetic relationship, or that type dissimilarity necessarily means lack of such relationship, has yet to be shown.

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AUREOMYCIN AND CHLORAMPHENICOL IN INFANTILE DIARRHOEA

BY

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The purpose of this communication is to describe briefly a preliminary trial of "aureomycin" and chloramphenicol in the treatment of infantile diarrhoea, or gastro-enteritis. Although diarrhoeal diseases of infancy have long been responsible for a considerable proportion of deaths in the first year of life, there is still no true understanding of their aetiology. Indeed, even definitions are difficult in the light of the diversity of views upon their pathogenesis. It is arguable whether diarrhoea of purely dietetic origin exists, and all cases which cannot unequivocally be assigned to other causes (such as coeliac disease or irritant poisons) should be regarded as infective even though the infective agent is as yet unknown. Nevertheless the acceptance of the infective nature of diarrhoea in infancy does not wholly solve the problem. It is usual to describe two groups: one in which the presumed infective agent is located in the alimentary tract (enteral infection) and for which there is very little direct pathological evidence, and the other in which it is located outside the alimentary tract (parenteral infection) and for which there is even less.

When one considers that the parenteral infection which is supposed to cause diarrhoea must apparently resolve itself into one of the upper respiratory tract, and that infections of the meninges and bones are not associated with diarrhoea, and even primary pneumonia and infections of the urinary tract by no means consistently so, it would appear that this distinction begs too many questions to be of real value. In all, there seems little justification for any more precise term than that of infantile diarrhoea, which is used here to indicate the non-specific diarrhoea of infancy. In this connexion it may be stated that only such established specific organisms as the *Shigella* and some *Salmonella* are excluded by this definition, and neither *Proteus vulgaris* nor the more recently incriminated varieties of *Bact. coli* are regarded as specific for the purposes of this communication.

Where a disease cannot be precisely defined it is particularly difficult to establish criteria of cure. Assessment of the result of any series of cases will inevitably depend to some extent upon largely subjective factors, such as the degree of severity and the presence or absence of parenteral infection, as well as upon factors that are administrative or social, such as the type of case admitted and the nature of the population from which the cases

are drawn. In the light of these considerations comparison between published series becomes extremely difficult. It seems not unlikely, moreover, that the difference between the series may be due as much to social and administrative factors as to the nature of the treatment of each, or perhaps even more. It is probable that real progress in the therapeutics of this condition must await a more precise understanding of the aetiological factors involved. Nevertheless, so serious a threat to the infant population must be met, and at the moment only empirical measures are possible.

Substances Used in Treatment

It is obvious that antibacterial substances had to be tried in infantile diarrhoea not only because the infective agent might have proved susceptible but also in order to deal with a parenteral infection, real or assumed. Sulphonamides were introduced early, and although opinion is divided (Campbell and Cunningham, 1941; Henderson, 1943; Hinden, 1948) it is usually conceded that they are of value in dealing with concomitant infections, while the use of compounds designed to have a local action on the bowel has on the whole been disappointing. The use of penicillin can be justified on the same grounds, and in particular when a concomitant infection, whether or not it is regarded as a cause of the diarrhoea, may well retard or jeopardize recovery. It is safe to say that neither the sulphonamides nor penicillin can be regarded as in any way specifically effective in the treatment of infantile diarrhoea.

The use of other antibiotics with a wider range of action offers an obvious advantage. On the accepted principle that concomitant infections should be dealt with, an antibacterial substance which combines the range of the sulphonamides with that of penicillin and which, moreover, can be administered by mouth is an obvious choice. In addition there is the not unreasonable hope that the infective agent itself might prove sensitive to one of the newer antibiotics. That rickettsiae and even some viruses have been shown to be susceptible lends countenance to this view (Long *et al.*, 1950).

Streptomycin was an early choice, and James, Kramer, and Armitage (1948) reported strikingly favourable results in the treatment of 30 cases of infantile gastro-enteritis with oral streptomycin. *Proteus vulgaris* was isolated on stool culture in most of these cases, but improvement was not confined to these. Both streptomycin and "polymyxin" were submitted to trial at this hospital and in various centres in Scotland under the aegis of the Scientific Advisory Committee of the Department of Health for Scotland. One may not anticipate the report of this trial, but our own experience was unremarkable.

Aureomycin would seem at first sight to have all the necessary qualifications as a wide-range antibiotic. It is effective against both staphylococci and coliform organisms, and has the obvious merit of obviating parenteral therapy. Moreover, the reported response of primary atypical pneumonia and ornithosis encouraged the hope that, even though the presumed infective agent in infantile diarrhoea should be a virus, for which there is already some evidence (Sabin, 1951), it might nevertheless respond to aureomycin. Its successful use in the treatment of infantile diarrhoea and vomiting has been reported from Stockholm (Magnusson *et al.*, 1950).

Chloramphenicol has many of the same advantages as aureomycin without, however, the same effectiveness against Gram-positive organisms (Long *et al.*, 1950). As these organisms are presumably not so likely to be implicated in infantile diarrhoea (although the concept of parenteral diarrhoea may not always permit this assumption, particularly in view of the prevalence of staphylococci in upper respiratory infections), and as chloramphenicol is more readily available in this country, it is to this antibiotic that most attention has been paid (Smellie, 1950; Cerruti and Scarzella, 1950). Smellie records 27 cases of infantile diarrhoea in which 75 mg. of choramphenicol per lb. (0.45 kg.) of body weight was given, this being continued for 10 to 12 days. All were seriously ill, and each patient except the one who died showed marked clinical improvement in two days. Cerruti and Scarzella also report encouraging results, using only 50 mg. per kg. body weight. In particular the incrimination of newly recognized varieties of *Bact. coli* in infantile diarrhoea has lent point to the use of chloramphenicol, to which they are sensitive.

Present Series

It was decided, therefore, to use first aureomycin and then chloramphenicol in the treatment of infantile diarrhoea as already defined. They were given in every second case admitted to one medical unit of the Royal Hospital for Sick Children, the others serving as controls. It should be made clear that of the cases of infantile diarrhoea seen at this hospital only those are admitted whose condition is so severe that out-patient treatment is considered quite unsuitable. Normally, therefore, only the more severe cases are admitted, and the average severity will be higher than that of the aggregate number seen. This is naturally reflected in the overall mortality. It was nevertheless convenient to classify all cases as mild, moderate, or severe. It will be remembered that these are relative terms.

Aureomycin was used from March to June inclusive, and chloramphenicol from July to October inclusive. Although the trial of chloramphenicol continues as part of an investigation into the distribution of the subvarieties of *Bact. coli*, it was felt that the clinical results were already conclusive enough as regards the major issue involved. It should be conceded that a really effective method of treatment does not require a very large series for its proof. What the physician who has charge of infants wants to know is whether the condition which he knows by the name of infantile gastro-enteritis is cured by aureomycin or chloramphenicol. To this question a relatively small series may well provide the answer.

Method

All cases were given the routine starvation regimen in use in this unit. On admission a clinical assessment of the child's condition and a note of any obvious parenteral infection were made. All feeds were withheld for at least twelve and usually twenty-four hours. During this time the child was given a mixture of molar sodium lactate and half-strength physiological saline in the proportion of 1 in 80. In children aged less than 4 weeks this solution is diluted with an equal amount of water. More concentrated solutions readily produce oedema in very young infants. If the condition of the child permitted, an attempt was made to rehydrate him by mouth before resorting to parenteral therapy. After a brief resuscitation in a warm cot the infant was offered this lactate-saline.

If, as often happened, the child was sick his stomach was gently washed out and 3–4 oz. (85–114 ml.) of lactate-saline was left in the stomach. Only if this failed was parenteral fluid given, and it is noteworthy that a large number of children who had all the appearances of severe dehydration, and who with less patient nursing would undoubtedly have required parenteral fluid, responded dramatically to these measures. Gastric lavage has been found a most effective measure against persistent vomiting. If parenteral fluid was required the intravenous route was used exclusively. The fluids chosen were human plasma followed by half-strength physiological saline containing molar sodium lactate in the proportion of 1 in 40 together with 5% glucose. In infants aged less than 4 weeks quarter-strength instead of half-strength physiological saline was used. The reintroduction of feeds was accomplished gradually with ½-oz. (14-ml.) feeds of half-cream National dried milk four-hourly (six times a day) for the first day and increasing by ½ oz. (14 ml.) a day. When the diarrhoea has ceased, sugar was added and the feeds were then adjusted to the child's requirements, including the changing over to full-cream National dried milk and the addition of mixed feeding if appropriate.

For the first four months of the trial every second case was given aureomycin in doses of 25 mg. per kg. of body weight in three or four divided doses (six- or eight-hourly) for seven days. The aureomycin was dispensed in 25-mg. powders and administered orally in small amounts of glycerin or honey. In addition, and probably unnecessarily, each child was given a 4-gr. (0.26-g.) tablet of Philip's yeast together with 50 mg. of ascorbic acid lest serious interference with bacterial synthesis of vitamins should lead to some deficiency. For the second four months of the trial chloramphenicol was used, again in every second case, in doses of 150 mg. per kg. of body weight a day in six divided doses (four-hourly) for seven to ten days. The drug was dispensed in 50-mg. powders and administered in the same way as aureomycin. A loading dose of 300 mg. per kg. of body weight was used.

The controls were given, in addition to the routine treatment outlined above, a sulphonamide and/or penicillin as indicated by their clinical condition. The absence of unequivocal evidence of a parenteral infection in a seriously ill child was not regarded as a bar to its receiving this treatment.

Results

Aureomycin.—During the period March to June inclusive, 34 cases (17 aureomycin, 17 controls) were treated, with an overall mortality of 14.7%. There were two deaths in the aureomycin-treated cases and three in the controls. The figures are given in Tables I–IV and show an analysis of the cases according to severity, age, percentage of expected weight, and average duration of stay in hospital. The last-named figure may be of more significance than the mortality, as the actual number of deaths in any one group is small. Of the two fatal cases treated with aureomycin, one is worthy of note in that, although the two stool cultures taken before death yielded no growth on the usual media, the diarrhoea persisted. Aureomycin had apparently dealt effectively with the intestinal bacteria without, however, benefiting the child. Of the three controls, one died within three hours and another within forty-eight hours of admission.

TABLE I.—*Classification According to Severity (Deaths in Parentheses)*

	Mild	Moderate	Severe	Total
Aureomycin ..	6 (—)	8 (1)	3 (1)	17 (2)
Controls	8 (—)	5 (—)	4 (3)	17 (3)
Total ..	14 (—)	13 (1)	7 (4)	34 (5)
Chloramphenicol	12 (—)	12 (2)	6 (2)	30 (4)
Controls	12 (—)	9 (—)	7 (3)	28 (3)
Total ..	24 (—)	21 (2)	13 (5)	58 (7)

TABLE II.—*Age Distribution (Deaths in Parentheses)*

	Under 4 Weeks	4–8 Weeks	Over 8 Weeks
Aureomycin ..	2 (—)	6 (1)	9 (1)
Controls	6 (2)	1 (—)	10 (1)
Total ..	8 (2)	7 (1)	19 (2)
Chloramphenicol ..	5 (—)	6 (2)	19 (2)
Controls	2 (1)	5 (—)	21 (2)
Total ..	7 (1)	11 (2)	40 (4)

TABLE III.—*Percentage Expected Weight on Admission (Deaths in Parentheses)*

	Less than 60%	60–75%	Over 75%	Over 100%
Aureomycin ..	3 (2)	4 (—)	10 (—)	
Controls	2 (—)	3 (1)	11 (1)	
Total ..	5 (2)	7 (1)	21 (1)	
Chloramphenicol	1 (—)	8 (—)	18 (4)	3 (—)
Controls	3 (1)	6 (—)	13 (—)	4 (—)
Total ..	4 (1)	14 (—)	31 (4)	7 (—)

Three patients who were critically ill on admission, and were not therefore weighed, are omitted from this table.

TABLE IV.—*Average Stay in Hospital of Non-Fatal Cases*

Aureomycin	12·1 days	Chloramphenicol ..	13·8 days
Controls	11·1 „	Controls	12·2 „

Chloramphenicol.—During July to September inclusive there were 58 cases, of which 30 received chloramphenicol, the rest being controls. The overall mortality was 12.1%. Four deaths occurred among the chloramphenicol-treated cases and three among the controls. Tables I to IV again give the relevant figures. Of the four fatal cases in the treated series one had a congenital malformation of the heart (complete transposition of the great vessels) and another had congenital syphilis. This latter case had been under treatment with penicillin for some weeks, and at necropsy there was little beyond some scarring of the liver to indicate the syphilitic infection.

Discussion

In each series there was a reasonable similarity between the treated cases and the controls. The proportion of severe cases, neonates, and marasmic babies, all factors influencing the outcome of infections, was much the same in each series. Indeed, the most striking feature of each set of figures is its similarity to the others. The mortality and average duration of stay in hospital show no significant difference between the three methods of treatment. So far as the mortality is concerned it is perhaps worth noting that of the 12 deaths three occurred within twenty-four hours of admission and a further two within sixty hours of admission.

The failure to demonstrate any striking difference between the results of the aureomycin and chloramphenicol groups and of the controls does not, of course, indicate that there are no virtues in the use of aureo-

mycin and chloramphenicol for the treatment of infantile diarrhoea, but merely that there is no evidence that they add anything to that already obtainable with a combination of a sulphonamide and penicillin. This in itself is sufficient to warrant the use of a single antibiotic instead of a combination of drugs. The choice between aureomycin and chloramphenicol would appear to depend as much upon the importance of staphylococci in this condition, and for which aureomycin would be necessary, as upon the coliform organisms which are sensitive to both. In this connexion one may mention that the use of sulphonamides and penicillin in infantile diarrhoea has caused a striking fall in the incidence of middle-ear infections found *post mortem*.

It seems unlikely that these results would be radically altered by merely increasing the number of cases, and it remains to consider the possible effect of the selection of cases. By definition, infantile diarrhoea in this series has been taken to include all cases of diarrhoea in the first year of life which were of non-specific origin. (In practice this excluded only dysentery and coeliac disease.) This wide definition was considered necessary in view of the difficulties of interpretation if any more precise distinctions were attempted. This is true whether the attempted distinctions are clinical, such as the separation of parenteral diarrhoea from enteral diarrhoea, or bacteriological, as in the differentiation of varieties of *Bact. coli*. Whatever the ultimate judgment upon these issues it is worth while to restate the fundamental difficulty in assessing the treatment of infantile diarrhoea. While the aetiology remains in doubt it is unlikely that a specific treatment will be found. Nevertheless it seems legitimate to conclude that the relative ineffectiveness of a wide range of antibacterial substances is strongly suggestive of a non-bacterial causation.

Summary

Aureomycin or chloramphenicol was used in alternate cases of a series of 92 consecutive infants admitted with infantile diarrhoea during a period of eight months. The controls were given penicillin and/or sulphonamides as indicated.

No significant difference was noted between either of the treated series and the controls. It is suggested that any wide-range antibacterial substance is likely to have a definite but limited value in the treatment of infantile diarrhoea. So far, however, it seems that no available antibiotic has a specific curative effect upon this disease. This may be regarded as an additional factor in favour of a non-bacterial causation of infantile diarrhoea.

I am indebted to Professor Stanley Graham, in whose wards these cases were treated, for generous criticism and advice in the preparation of this paper. I am grateful to Dr. A. M. MacDonald and his staff for bacteriological reports and necropsies. To Sister Sutherland and the nursing staff my thanks are due for a consistently high standard of nursing.

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PHAEOCHROMOCYTOMA PRESENTING AS AN ABDOMINAL EMERGENCY

BY

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Phaeochromocytoma is now being recognized more frequently, not only in patients whose clinical features suggest paroxysmal hypertension (Walton, 1950) but also in those whose presenting disability is sustained hypertension (Green, 1946) or diabetes mellitus (Duncan *et al.*, 1944; Goldner, 1947). This clinical diagnosis is usually suggested by the association of two features—a liability to attacks, with palpitations, headaches, and sweating, and evidence of hypertension either persistent or observed during these attacks. In the present case, which was under observation for 18 hours, the clinical picture was dominated for that time by a state of shock with periodic exacerbations associated with severe abdominal pains. The blood pressure was either normal or subnormal, and the E.C.G. and *x*-ray film showed no evidence of previous hypertension. This case is reported because of its unusual presentation, which served to emphasize that the condition of shock, familiar as a post-operative or post-manipulative complication in these patients, may be the presenting clinical problem, thus masking any evidence of previous hypertension.

Case Report

A carpenter aged 29 was admitted to hospital as an emergency case of pneumonia. He had been ill for 24 hours and had become distressed and prostrate, unable even to sit up, coughing up large amounts of blood-stained sputum.

He gave a history of being suddenly struck down the day before with aches and pains all over, and complained particularly of headaches and pains in the abdomen, back, and chest. He said that for the past four months he had had an unproductive cough, which he thought brought on vomiting once or twice a day. With the vomiting he had headache, palpitation, and profuse sweating. On this account he had attended another hospital, where he had had a barium meal and was assured that he was suffering from "nerves." He had lost no weight and had been able to carry on with his work. Further details were not then available, but it was subsequently discovered that he had previously complained of attacks of vomiting, unrelated to meals, occurring almost every night. Headaches, palpitations, and profuse sweating accompanied the vomiting. On the two occasions it was tested his blood pressure was found to be normal. After treatment with phenobarbitone he seemed a little improved and had ceased attending.

On admission he was found to be a robustly built young man, limp, and ashen grey in colour; he was coughing up copious blood-stained sputum, and vomited and sweated profusely. His temperature was 96° F. (35.6° C.), pulse 100, and respiratory rate 30. His blood pressure at this time was 160/80. There were many fine crepitations, especially in the apical regions. There was tenderness in the epigastrium, especially on the left, and in the left renal angle. The urine

showed sugar (orange to Benedict's test), 1 + of albumin, 2.3 g. of chloride per litre, and no pus or blood cells. His E.S.R. was 2 mm. in one hour.

A few hours after admission he was suddenly seized with excruciating abdominal pains, starting in his left flank, severe enough to cause him to roll about the bed in agony. He became suddenly shocked, his blood pressure being unrecordable in either arm, and the whole clinical picture was dominated by collapse, anxiety, and restlessness.

A blood sample removed at the height of the attack was found to contain plasma sodium, 331 mg. per 100 ml.; urea, 57 mg. per 100 ml.; glucose, 121 mg. per 100 ml.; alkali reserve, 49.4; and serum amylase, 115 units per 100 ml. Chest and abdominal *x*-ray films and E.C.G. were normal. His haemoglobin was 112%, W.B.C. 27,000 (88% polymorphs). He was thought to have either a small strangulation or a retroperitoneal haemorrhage of unspecified origin. Our surgical colleagues agreed, and exploration was decided upon after recovery from shock.

In a short while he vomited and became somewhat eased, his blood pressure now being 100/75. In two hours he had to a great extent recovered. His chest signs had completely disappeared and he complained only of tenderness in the left loin.

Two hours later he had a further episode of agonizing pain in the left loin, accompanied by vomiting, during which his extremities were cold, cyanosed, and excessively sweaty. His blood pressure was 110/85. Morphine ¼ gr. (16 mg.), and atropine, 1/100 gr. (0.65 mg.), made him more comfortable, but, in view of a suddenly rising pulse rate reaching 150 a minute, immediate intervention was considered essential. His blood pressure during anaesthetization rose to 170/120.

Operation Notes.—"The abdomen was opened through a left paramedian incision. There was no free fluid in the peritoneal cavity, and no coils of distended small or large bowel were encountered. Medial to the kidney and lying retroperitoneally could be felt a tense rounded tumour the size of a tennis ball. It did not pulsate. The peritoneum on the anterior aspect of the left kidney was incised and the kidney was found to be normal in size, shape, and position. During the delivery of the upper pole of the kidney there was a gush of blood followed by the discharge of several grammes of fragmented heavily blood-stained tissue which looked like a degenerating tumour. At this stage the patient's pulse became impalpable and the pulse rate went up to an unrecordable level. The abdominal wall was quickly closed in layers without drainage. A drip was set up and a concentration of 1 in 500,000 adrenaline was given. This was supplemented by 30 ml. of 'eucortone.' The systolic blood pressure at the end of the operation was 100 and the pulse was still virtually unrecordable. He was sweating, the skin was cold, and his lips were greyish blue. He remained in this condition for about 10 minutes and then expired."

Pathology.—At necropsy a tumour, 5 by 4 by 1.5 in. (12.5 by 10 by 3.75 cm.) was found in the left adrenal gland; little else abnormal was seen apart from congestion of the lungs and spleen and slight cardiac hypertrophy. The microscopical appearance showed the tumour "to be made up of irregularly shaped large cells, in places syncytial, with large vesicular nuclei. Most possess a deeply vacuolated cytoplasm. A few tumour cells show brown pigment granules. Mitoses are infrequent. This histology is typical of a phaeochromocytoma."

Discussion

The analysis of the dramatic disaster which overtook this young man seems clear in retrospect, but the diagnosis was baffling at the time.

The clinical picture was dominated during his brief period under our care by recurring episodes of shock, with low blood pressure and abdominal pain. We had no evidence of his state before admission; his E.C.G. and *x*-ray films were within normal limits; and, indeed, no indisputable evidence of hypertension was obtained until preparations were in hand for exploratory laparotomy, as an acute abdominal emergency. The epigastric discomfort, hypotension, and vomiting led us to consider Addisonian crisis, though there was little suggestive in his sketchy history, no pigmentation or evidence of dehydration; and the relatively normal blood chemistry disposed of this suggestion. Diaphragmatic hernia with obstruction was considered, as was renal colic; the negative *x*-ray findings and the absence of blood and pus in the urine weighed against these. Acute haemorrhagic pancreatitis was thought to be unlikely in view of the excellent interval recovery from his episodic states of shock and the low plasma amylase.

In cases of phaeochromocytoma, shock following operation or manipulation is frequently recorded; but when it is the presenting condition, as in this case and in one case described by Wilkins *et al.* (1950), diagnosis is difficult. It is possible that the haemorrhage into the tumour in this patient accentuated the degree of his shock, and it was no doubt responsible for much of the localized pain in the left loin. When admitted he was suffering from acute left ventricular failure and pulmonary oedema, and had suffered for some months from similar attacks. It was difficult to accept this interpretation at the time, without evidence of a cause for heart failure, with a normal blood pressure and jugular venous pressure, and no abnormality other than tachycardia in the intervals between his acute exacerbations of shock. Wells and Boman (1937) have drawn attention to this possibility, and indeed in one of the first cases to be recorded (Labbe *et al.*, 1922) the patient died in this manner.

The diagnosis of phaeochromocytoma was considered, but unfortunately was discarded, as there was no evidence of previous hypertension by sphygmomanometer, ophthalmoscope, chest *x*-ray film, or E.C.G. Attention has been directed to the frequency of vomiting in attacks of paroxysmal hypertension. Washington *et al.* (1946) record a case which presented because of vomiting every five or six days. Rabin (1929) records the case of a patient who vomited almost every night, as our patient had done when he reported to the other hospital. Wells and Boman found that vomiting was occasionally induced to relieve the symptoms, as it indeed appeared to do in the second episode observed in our patient. The profuse sweating and peripheral vasoconstriction on the second attack in the ward should have indicated an outpouring of adrenal medullary substance (Smithwick *et al.*, 1950). Moreover, we should have taken more account of his unexplained glycosuria and his slightly raised fasting blood sugar of 120 mg. per 100 ml. Rabin drew attention to the presence of unexplained glycosuria in these cases. Occasional cases have no evidence of hyperglycosuria even in an attack (Pantridge and Burrows, 1951), but in most of the cases studied there has been an elevated diabetic-like glucose-tolerance curve, sometimes without glycosuria (Wilkins *et al.*, 1950) and sometimes with frank diabetes (Duncan *et al.*, 1944; Goldner, 1947).

This case also raises the most important therapeutic problem of phaeochromocytoma—how to prevent the shock which may supervene as a result of severe hypertensive attacks, whether spontaneous or after surgical or other manipulation of the tumour.

Effective adrenergic blocking agents able to prevent the hypertensive attacks have been described (Console *et al.*, 1950) and their severe side-reactions discussed (Swan, 1951). Some, such as benzodiozane, act quickly and are useful in the acute hypertensive attack whether spontaneous or provoked by histamine. Others, such as "dibenamine," are slower to act but more prolonged and complete in action, and preliminary reports (Bartels and Cattell, 1950; Crowther, 1951) suggest that these probably offer the best hope of success in preparing the patient for later surgery by preventing the state of shock.

We are grateful to Dr. Russell Fraser and Mr. M. R. Ewing for permission to publish the case, which was under their care.

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HEPATIC COMA WITH RECOVERY IN A CYSTINURIC

BY

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Recovery from hepatic coma is always an event of note. Latner (1950) reported the recovery of four out of five consecutive cases on his regime. Because no one physician is likely to see more than an occasional case of hepatic coma it is important to establish whether these results can be substantiated in other hands in a syndrome in which effective therapy has been conspicuously absent. Communication to Latner or to the medical press of all results of the use of his regime, whether favourable or not, would seem desirable.

It has been suggested that cystine deficiency may be a factor in human liver disease (Himsworth, 1945; Glynn, Himsworth, and Neuberger, 1945). The following case is therefore of especial interest in that one would think a cystinuric, losing as he does fair quantities of cystine continuously into his urine, would be most susceptible to liver disease. This case does not support that idea.

Case Report

The patient was a male physician aged 42 in good health. He had never had jaundice, but had recently attended a jaundiced pregnant woman. On October 10, 1951, he felt feverish and went to bed. Two days later jaundice developed. His fever resolved in a further two to three days, the jaundice increased, and he began to vomit. The vomiting increased in severity until on the sixth day of his illness he could not retain water by mouth. Seen next day, he appeared very depressed and quiet, although mentally alert. He was markedly jaundiced. His liver was easily palpable but not very tender. He had a moist furred tongue and took water and glucose fluids well. He took 100 mg. of pethidine that night because he "could not get mental relaxation," and in the early hours of the following day (eighth day) he took 1½ gr. (0.1 g.) of "seconal" (usual sedative). He then slept deeply and all that day remained drowsy. Fluids were taken well, and he passed 3½ pints (2 litres) of urine. In the early hours of the ninth day, for the first time, he behaved rather oddly—pushing his wife away when getting out of bed.

When seen that morning (October 18) he lay quiet and comatose, unable to recognize relatives or to answer questions. His pupils were widely dilated. He was deeply icteric, with no petechiae. His liver was not palpable, but his respirations were shallow. There was no rise in jugular venous pressure. His blood pressure was 140/90. Ascites was not present. He was admitted to the Lister Hospital as an urgent case and placed on the Latner regime. This consists of two solutions: (*a*) 10% dextrose in normal saline, to each pint (570 ml.) of which are added 50 mg. of thiamin hydrochloride, 150 mg. of nicotinamide, 50 mg. of riboflavin, and 0.5 g. of potassium chloride; (*b*) plasma to which vitamins as in (*a*) but no potassium chloride have been added.

Four pints (2.3 litres) of the dextrose-saline solution were given in 24 hours, but only one pint (570 ml.) of plasma was given (October 19, morning) during the 50 hours in which the intravenous drip was running. Latner recommends three pints (1.7 litres) of dextrose-saline, followed by one pint (570 ml.) of plasma in every 24 hours. There were administered in addition to the intravenous drip: 300 mg. of tocopherol (100 mg. thrice daily) intramuscularly, 60 mg. of vitamin K daily, and 1,000,000 units of penicillin daily.

On the day of admission the patient remained very drowsy and became very restless, necessitating three 5-ml. doses of paraldehyde intramuscularly in the first 24 hours. The next day (October 19) his condition appeared very much the same (coma and restlessness). However, when examined at 5.45 p.m. he just opened his eyelids, and by 8.15 p.m. had become fairly orientated and alert. The intravenous drip was discontinued, after 50 hours, on October 20. During this time he had had 9 pints (5.1 litres) of fluid by drip (glucose 450 g., sodium chloride approximately 12 g.) and 55 oz. (1.6 litres) of fluid by mouth. He was now given tocopherol, B vitamins, and "hepovite" by mouth (Latner). From this time onwards recovery proceeded without significant episodes. He left hospital on November 7 and returned to work on January 8, 1951, feeling very well.

Laboratory Data.—On the day of admission serum bilirubin was 4.8 mg. per 100 ml., thymol turbidity 14 units, prothrombin time 27% (24 seconds), alkaline phosphatase 13.7 units, serum proteins 5 g. % (albumin 3.4 g., globulin 1.6 g.), Hb 106%. Urine examination showed bilirubinuria, urobilinogen and urobilin absent, with a trace of albumin and a few granular casts. The serum bilirubin rose to 8.2 mg. per 100 ml. two days later and to 12 mg. after one week. By December 1 it had fallen to 1 mg. per 100 ml. and by December 29 to 0.8 mg. Thymol turbidity, which lay between 14 and 10 units in the first week, fell steadily to 4.5 units on December 29. Urobilinogen and urobilin (Ehrlich and Schlesinger tests respectively) were present in quantity for the first time on November 1. The haemoglobin was 110% on November 3. On December 5 total proteins were 8 g. % (albumin 6 g., globin 2 g.).

Paper Chromatography

At the height of coma (October 18) a specimen of urine was sent to Dr. C. E. Dent through the kindness of Dr. S. P. V. Sherlock. It showed a slight generalized amino-aciduria with abnormal quantities of cystine, lysine,

and ethanolamine on paper chromatography. A further specimen of urine on December 29, when the patient was fully convalescent, showed abnormal quantities of cystine, lysine, and methyl histidine, but was otherwise normal.

Dr. Dent interprets these findings as follows. The first specimen (October 18) was compatible with severe liver damage, but not so severe as would be regarded as inevitably fatal. It also suggested that the patient was a cystinuric. The second specimen (December 29) confirmed the fact that he was a true cystinuric—that is, was one of those people who all their lives excrete in the urine exceptionally large quantities of cystine, lysine, and sometimes also arginine (Dent and Rose, 1951). The increased quantity of methyl histidine cannot yet be interpreted.

Summary

A record is given of a case of infective hepatitis developing coma which recovered after 36 hours. The Latner regime of therapy was used.

The patient showed a slight generalized amino-aciduria to paper chromatography at the height of coma. It was a surprise to find that he was a cystinuric, a fact which was confirmed later when he was convalescent. The significance of this is briefly discussed.

I am greatly indebted to Dr. C. E. Dent, of University College Hospital, for his collaboration and for permission to use his data and observations.

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Medical Memorandum

A Successful Case of Intra-arterial Blood Transfusion

We understand that intra-arterial blood transfusion has been used in certain Continental countries, but have seen little reference to it in South African or British literature. It has several theoretical advantages over intravenous transfusion, particularly when blood is needed urgently. The blood supply to the vital cerebral centres and to the coronary arteries is directly dependent on the pressure in the aorta, and it seems that transfusion into an artery raises this far more quickly than intravenous transfusion. In the dog (Samson Wright, 1947) an increase in mean aortic pressure from 50 to 130 mm. Hg may increase the flow in the coronary arteries from 20 to 250 ml. a minute. In our case, soon after the transfusion started the aorta appeared bulging and distended, and it was obvious that the pressure within had been substantially raised. It would also seem that the risk of pulmonary oedema due to overloading the right side of the heart should be much diminished.

An essential requirement of the method is that the blood should be perfectly free of clots, otherwise there must be a considerable risk of emboli lodging in the arteries of the extremities or elsewhere. There is no longer the filtering action of the lungs as in intravenous transfusion.

When we applied the method to our case all concerned were convinced that she was moribund, and we believe that intravenous transfusion, even at the same speed, would not have saved her life. A tribute is due to the nursing staff for producing the necessary apparatus with such rapidity.

Case Report

The patient, a moderately obese woman aged 68 with carcinoma of the cervix infiltrating the bladder and rectum, was brought to the theatre to undergo the operation described by Brunschwig in which a complete pelvic clearance is carried out. The stages of the operation are as follows: panhysterectomy with excision of bladder, urethra, labia minora, rectum, followed by transplantation of ureters into the sigmoid colon and a colostomy. Her pulse was 76; blood pressure 150/90. A blood transfusion into the right leg was set up. Premedication with "omnopon," 1/3 gr. (22 mg.), atropine, 1/100 gr. (0.65 mg.), was given one hour before operation. Anaesthesia was induced with thiopentone and maintained on nitrous oxide and oxygen with ether and the addition of fractional D-tubocurarine chloride. An oral endotracheal tube was passed.

For the first two hours of operating time the patient's condition was quite satisfactory. There was a slight rise in pulse rate and a slight fall in blood pressure. However, during the process of stripping the pelvic wall, difficulty was encountered in controlling bleeding. At this stage the haemorrhage became very profuse indeed. Within a few minutes the patient became very pale, the skin cold and moist, and the pulse at the wrists and temple unobtainable. Auscultation failed to reveal any heart sounds. Automatic respiration also ceased.

Artificial respiration with 100% oxygen was immediately instituted. Although the blood transfusion into the patient's leg was running at a fair speed she did not show any signs of recovery. Repeated injections of methylamphetamine hydrochloride ("methedrine") produced no response.

The surgeon was able to feel feeble rapid pulsation in the abdominal aorta. One of us at this moment set up another blood transfusion apparatus with all possible speed. The surgeon was provided with sterile rubber tubing and a large needle (aspirating needle, gauge 14) and requested to insert the latter into the common iliac artery with the end pointing towards the heart. The blood was now pumped in at high speed and within 10 minutes a litre had been given.

During this short period a remarkable recovery occurred. The patient started automatic respiration and a fairly good pulse was palpable at the wrist and temple.

The operation was completed. Oxygen was administered continuously until consciousness was regained. The patient left the theatre with a pulse of 90 and a systolic pressure of 65. During transport to the ward some two hours after the intra-arterial transfusion her condition deteriorated slightly. There was some bleeding per vaginam. She was put into bed in the Trendelenburg position and given oxygen and omnopon, 1/6 gr. (45 mg.) intravenously.

A fortnight after the operation the patient was making good progress and there was no sign of mental impairment, nor were there any respiratory complications. There was, however, some bowel atonia for about a week.

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A note in *Nature* (July 14, page 86) discusses the possibility that the colour sensitivity of the human eye is influenced by the physical position of the observer. Usually, when the observer is in the erect position, both eyes show the same colour sensitivity, but if he lies on one side a difference between the colour responses of the two eyes develops; the lower eye becomes markedly red-sensitive compared with the other. When he turns on to his back the two eyes resume their original similar response, and by turning on to the other side the formerly red-sensitive eye, now uppermost, gradually develops blue-sensitivity.

Reviews

BIOLOGICAL KNOWLEDGE

A History of Biology. A General Introduction to the Study of Living Things. By Charles Singer. Revised second edition. (Pp. 579; 194 illustrations. £1 15s.) London: H. K. Lewis and Co. 1950.

Professor Singer has produced a memorable work, as we were entitled to expect from our leading authority on the history of biology. No one but himself could have written it, and, although he modestly admits that he cannot, of his own knowledge, cover the whole area of the subject of which he treats, his attempt to do so has been remarkably successful. In fact his work is not only invaluable to the student, but has its admonitions for the historian himself. He believes that, although no man can grasp the nature of all branches of science, yet it is possible to envisage the picture of nature as revealed by scientific research as clearly to-day as in previous ages. "It would," he claims, "be a poor sort of science that made the world less and not more intelligible." Hence the bias of this book is to give a picture of the state of biological knowledge as a whole, and to lead up to the study of biological problems. Omissions and inclusions have to be decided, and, in summing up, the criticism of the working man of science must be met and withstood. The "temerarious intervention of the historian in domestic differences will not fail to call down upon him the imprecations of those from whom he differs, while his ignorance may draw upon him the derision of those with whom he agrees."

We do not quite sympathize with Professor Singer in his views on the methods of historical scientific research. All research should be undertaken only by historians who have also at first hand a detailed working knowledge of the modern subject. Such knowledge is a first essential in the business. They must be prepared to check the statements and conclusions of the old masters, and able to form a sound judgment of their value. For example, when a reputable comparative anatomist declares that the cavities of the valves of the jugular veins of the barbary cow are directed, not towards the heart, but towards the head, it is not sufficient to reject so unexpected a statement on *a priori* grounds, but the actual conditions must be explored and discovered. Hence any historian of science should be equipped so as to bring modern knowledge of fact and theory to bear on his studies. Moreover, the work of such men must inevitably form the raw material on which the pontiffs base their inspired pronouncements.

Professor Singer's work is divided into three parts: (1) the older biology; (2) the historical foundations of modern biology; (3) emergence of main themes of contemporary biology. These divisions include the rise and fall of ancient science and the renaissance of modern science; early museums; the great seventeenth-century naturalists and the rise of classificatory systems; the comparative method; distribution in time and space; evolution; cell doctrine; vitalism and mechanism; comparative physiology; biogenesis and abiogenesis; embryology and the biogenetic law; sex; theories of heredity.

The work is well printed, and the literary style has the vigour, clarity, and eloquence characteristic of Professor Singer's writings. The index is confined to the names of authorities quoted.

F. J. COLE.

MALIGNANT DISEASE IN GYNAECOLOGY

Malignant Disease of the Female Genital Tract. By Stanley Way, M.R.C.O.G. (Pp. 279; 38 illustrations. £1 4s.) London: J. and A. Churchill. 1951.

Mr. Stanley Way has attempted to give a short account of malignant disease of the female genital tract in such a way as to render down the vast literature on the pathology, clinical aspects, and treatment into a small compass. The author must be commended for his courage, for he states in his preface that he knows full well the great difficulties, and a condensed book of this kind is always open to criticism in detail. The highest praise should be given for the efficiency with which he has dealt with the sections on carcinoma of the vulva and carcinoma of the uterus. He has quite rightly emphasized his own work on carcinoma of the vulva and the interest he has taken in the radiation histology of Gluckmann and Spear. The illustrations are excellent.

He includes a remarkably able and interesting chapter on pregnancy complicated by malignant tumours. The chapter on sarcoma of the genital tract is well below the standard of the rest of the book, and the section on carcinoma of the ovary is far too elementary. The lymphatic drainage of the labia majora and of Bartholin's gland might be described with some mention of the work of Peham Amreich, and the incidence of the inconstant nodes of the mons and of the inguinal canal should be given if possible. On the other hand, the author very properly emphasizes the definition of the obturator node, but makes no reference to the frequency with which the anatomical node is infiltrated in carcinoma of the cervix. The vault metastases after hysterectomy for carcinoma of the body of the uterus and the doubts which exist in the author's mind about their aetiology might be elaborated.

The literary style is lively, although some of the comments may irritate more sober-minded members of the profession. In its present form the book will probably be of service to senior students and practising gynaecologists, but it must surely be regarded as a stepping-stone to a more comprehensive contribution. It is hoped that the author will expand the book in the next edition and make it more comprehensive.

WILFRED SHAW.

HYPNOSIS

Clinical Applications of Suggestion and Hypnosis. By William T. Heron, M.A., Ph.D. (Pp. 116. £1 2s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1950.

A good deal of interest has been shown lately in the possible uses of hypnosis in ordinary medical practice. This little book, published at a price which is very high for the British reader, provides a useful aid. While the author discusses the general aspects of hypnosis in a way which gives a sufficient introduction, he focuses attention mainly on the practical problems of technique—how to approach the patient, the degrees of the hypnotic state, methods of induction, post-hypnotic suggestion, and precautions. The author is not a medical man, but is professor of psychology in the University of Minnesota, and seems to have had a good deal of experience with patients. He has much to say about the use of hypnosis to attain minor degrees of surgical anaesthesia—as, for instance, may be called for in dentistry.

Medical men who are interested in hypnosis might well make more use of it in general practice than they

do at present. It is not a difficult technique, and in its ordinary applications demands no great knowledge of psychiatry. The use of hypnosis in psychotherapy would require training and experience, but is a highly specialized field of application. Probably the easiest method by which acquaintance with the technique could be obtained would be by making the first trials not with adults but with children. The author has some useful guidance to give about the management of suggestion in its simplest forms, and suggestion is constantly given by any competent practitioner in his daily handling of patients.

ELIOT SLATER.

TEXTBOOKS FOR HEALTH VISITORS

Health Visiting. By Margaret McEwan, M.B.E., S.R.N., S.C.M. (Pp. 383; 5 charts. 18s.) London: Faber and Faber. 1951.

Textbook for Health Visitors. By Llywelyn Roberts, M.D., M.R.C.P., D.P.H., Beryl Corner, M.D., M.R.C.P., and I. G. Davies, M.D., M.R.C.P., D.P.H. (Pp. 551; illustrated. 21s.) London: Baillière, Tindall and Cox. 1951.

Two textbooks on the same subject, with bindings of similar hue, "drop like the fruits of the tree" into the lap of the health visitor more or less simultaneously. One such textbook has been much needed; two represent not a surfeit but a sufficiency; both will be welcomed in particular by health-visitor tutors and their students and by public health nurses generally.

Miss McEwan has brought her wide knowledge and experience in the training of health visitors to the task of writing a book which is modestly claimed to be an introduction to the work of the health visitor. It is much more than that: it is a storehouse of reliable information and sound comment which is easy to read and will take the health visitor student a long way in her heavy course of training, and she will wish to keep it by her when she is fully fledged. The section on the history of health visiting is sound and concise, and the various types of administrative authorities are clearly described. The bibliography is most helpful and the index well selected and accurate. Social legislation is interpreted simply and skilfully.

Three members of the Royal College of Physicians have combined to produce a larger and more comprehensive textbook designed for the health visitor in training and other health workers. It is well written, and the publishers are to be congratulated on the attractiveness of the format. There are numerous plates, charts, and diagrams—all well done. The chapter on infectious diseases is as useful as it is extensive, and those on the management of the baby and infant feeding are clear and practical. Food and the principles of dietetics are also well discussed, and I know of nothing better for rapid and easy reference in these rather extensive subjects. This excellent textbook is unfortunately marred by an index which, subjected to random sampling, all too soon revealed some irritating errors. And somehow "voluntary patient" has been substituted for "temporary patient" in a section of an interpretation of mental treatment legislation—certainly confusing and probably misleading to most readers.

Neither book covers completely the syllabus for the health visitors' examination, nor could either be regarded as a complete work of reference on the subject of health visiting. But it is doubtful whether any single textbook could cover the ground completely and still remain readable and within reasonable compass. In subsequent editions the authors of these textbooks would be well advised to consider the advantage of discussing much more extensively the principles of teaching, in order to help the health visitor to become a good health educator. Both books are to be commended, and social workers will read them with profit and keep them as worthy additions to their library

C METCALFE BROWN.

SIR HENRY THOMPSON

The Versatile Victorian. Being the Life of Sir Henry Thompson, Bt., 1820–1904. By Zachary Cope, M.D. (Pp. 179; illustrated. 12s. 6d.) London: Harvey and Blythe. 1951.

In his account of Sir Henry Thompson, Mr. Zachary Cope has produced a brilliant study of the social and medical world of the Victorian era, and of a man whose versatility resulted in a life of extraordinary interest. The author was fortunate in having at his disposal a large amount of material left by Thompson, practically constituting a detailed diary of the whole of his life, and he has made such admirable use of it that the result has all the interest of an autobiography. Born in 1820 and living in full vigour to the age of 84, Thompson covered a very remarkable period, and in the great progress of surgery in that period he had an ample share. Among his patients he numbered the King of the Belgians and Napoleon III, and he was the intimate and valued friend of successive members of our own royal family. Moreover, in a society which is now, alas, only a memory, he was an artist of some distinction and a social leader in the world of art and science.

We would congratulate the author on having found a subject so peculiarly suited to his own genius and on the production of a study fascinating from so many aspects. He has supplied a really valuable addition to our knowledge of an important period, and he has given us a story to which for variety of interest it would be difficult to find a parallel.

HENRY SOUTTAR.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

A Laboratory Guide to the Anatomy of the Rabbit. By E. H. Craigie. (Pp. 113. 21s.) London: Geoffrey Cumberlege. 1951.

A Pathology of the Eye. By E. Wolff, M.B., B.S., F.R.C.S. 3rd ed. (Pp. 364. 55s.) London: H. K. Lewis. 1951.

Heart Disease. By E. Goldberger, B.S., M.D. (Pp. 651. 70s.) London: Henry Kimpton. 1951.

The Dentists Register, 1951. Published by the Dental Board of the United Kingdom. (Pp. 429. 18s.) London: Constable. 1951.

Studies in Lobotomy. Edited by M. Greenblatt, M.D., and others. (Pp. 495. 63s.) London: William Heinemann. 1951.

Disease in Infancy and Childhood. By R. W. B. Ellis, O.B.E., M.A., M.D., F.R.C.P. (Pp. 695 42s.) Edinburgh: E. and S. Livingstone. 1951.

Collected Papers of the Middlesex Hospital Medical School, 1949-50. London: Middlesex Hospital. 1951.

Kurzes Lehrbuch der Enzymologie. By Professor T. Bersin. 3rd ed. (Pp. 274. M. 19.20.) Leipzig: Geest and Portig. 1951.

Lehrbuch der Chirurgie. Edited by Professor Gohrbandt and others. Vols. 1 and 2. 10th ed. (Pp. 1,600. M. 98.) Jena: Gustav Fischer. 1951.

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BLACKWATER FEVER

Few morbid conditions have been the subject of so many conjectures as blackwater fever. During the past hundred years the output of papers discussing it has been unceasing, though many of the views advanced, having no foundation of scientific observation or experimental fact,[1] have little to commend them beyond their ingenuity. It has been said with truth that the putting forward of theories about the causation of blackwater fever is a function inversely proportional to knowledge of the established facts, and the ordinary doctor may well become lost in a fog of surmise.[2] The association of blackwater fever with malaria was recognized by French[3-5] and American[6 7] writers a hundred years ago, and in America it was actually known at that period as malarial haematuria. For some years there was a controversy about the nature of the colouring matter in the urine, and it was not until 1878 that this was shown to be due to haemoglobin and not to blood or bile.[8] The fact that the syndrome could be precipitated by quinine was known to Greek observers as far back as 1858,[9] but it was also early recognized that residence in a malarious country was an almost invariable antecedent.[10] That quinine was not the sole precipitating factor was demonstrated by A. Plehn[11] in 1896 and at about the same time by several other observers[12] who recorded a number of cases in persons who had never taken the drug. Blackwater fever has been described in patients under treatment with induced *P. falciparum* infections for neurosyphilis.[13 14] In all cases reported the condition supervened after the subjects had experienced repeated recrudescences of fever over a period of several months.

In 1898 Thayer[15] suggested that the red cells in blackwater fever became less resistant than normal to changes in the osmotic tension of the plasma, and were thus liable to undergo solution. Stephens and Christophers[16] investigated the behaviour of the red cells in different strengths of salt solution and found that during an attack of blackwater fever the cells might even show an increased resistance. They suggested that this might be due to the destruction of the weaker cells, so that only the most resistant remained after the attack. During the early years of the present century Italian writers put forward the view that malarial haemoglobinuria was due to the action of a specific haemolysin, and Casagrandi[17] claimed to have demonstrated the existence of such an agent in the blood, masked by the presence of an anti-haemolysin. This finding is in harmony with a more recently expressed contention that the lysis is a manifestation of excessive uninhibited activity of a normal lytic process.[18] The existence of a haemolysin has been postulated by many other observers, some maintaining that lysis takes place within the red cells,[19] others that it is extracellular[20]; but the question about what actually brings about the lysaemia remains unanswered.[21] Fairley and Bromfield[22] found evidence to suggest that lysis was mainly intravascular, the plasma methaemoglobin being apparently derived from the haemoglobin of the lysed cells. They also observed a further peculiar haemoglobin derivative, now known as methaem-albumin, which occurs constantly in the blood in blackwater fever but does not pass through the kidneys. A suggestion that Rh factors are concerned in the haemolytic process has been put forward but lacks confirmation.[23]

From time to time it has been alleged that blackwater fever is due to the action of some specific organism or haemolytic strain of *Plasmodium*, but there is overwhelming evidence against the validity of such a theory.[21] A suggestion that the exciting cause is acute dissolution of malaria parasites[24] or the discharge of parasitized red cells by contraction of the spleen[25] is discounted by the fact that parasites in the peripheral blood are usually very scanty and often too few to be demonstrable in smears made at the beginning of an attack; while spleen puncture at this stage has shown that here, too, parasites may be scanty or absent.[1] This last observation also tends to disprove the view sometimes expressed that the parasites in blackwater fever are concentrated in the internal organs.[26] A theory advanced by A. Plehn[27] that the primary lesion in blackwater fever is a profound change in the renal epithelium was challenged

1 Yorke, W., Murgatroyd, F., and Owen, D. U., *Trans. roy. Soc. trop. Med. Hyg.*, 1930, **23**, 335
2 Christophers, S. R., 1937. Foreword to Stephens.[24]
3 Lebeau, 1851, Thèse, Paris.
4 Le Roy de Méricourt, A., 1853, Thèse, Paris.
5 Daullé, D. J., 1857, Thèse, Paris.
6 Cummings, J. C., *New Orleans med. News Hosp. Gaz.*, 1859–60, **6**, 811.
7 Osborn, J. D., *New Orleans J. Med.*, 1869, **21**, 61.
8 Corre, A., *Arch. Méd. nav.*, 1878, **29**, 393.
9 Veretas, D., *Soc. Méd. Grecque Paris*, 1858, Nov. 6.
10 Bérenger-Féraud, L. J. B., *De la Fièvre Bilieuse Mélanurique des Pays Chauds*, 1874. Paris
11 *Beiträge zur Kenntniss von Verlauf und Behandlung der tropischen Malaria in Kamerun*, 1896, Berlin.
12 Cited by Laveran, A., *Traité du Paludisme*, 1907, Paris.
13 James, S. P., Nicol, W. D., and Shute, P. G., *Proc. roy. Soc. Med.*, 1932, **25**, 1153
14 Kitchen, S. F., and Sadler, G. G., *Amer. J. trop. Med.*, 1945, **25**, 379.
15 *Malarial Fevers*, 1898, New Haven.
16 Rep. Malar. Comm. roy. Soc., Series 1 and 5, 1900–1901, London.
17 *Atti Soc. Studi Malar.*, 1906, **7**, 115.
18 Maegraith, B. G., Findlay, G. M., and Martin, N. H., *Lancet*, 1943, **1**, 573.
19 Yorke, W., and Barratt, J. O. W., *Ann. trop. Med. Parasit.*, 1909, **3**, 1.

by Yorke and his colleagues,[1] who contended that the histological changes in the kidney are not primary but are a consequence of the excretion of haemoglobin. This is sometimes known as the "mechanical blockage theory" and was first put forward by Baker and Dodds[28] in 1925. Maegraith and Findlay,[29] however, and others have pointed out that oliguria and anuria occur in many different clinical conditions, and suggest that the basis of kidney failure in blackwater fever may be due not to the presence of circulating pigment but to renal anoxia arising from a redistribution of the renal blood flow, which results in the by-passing of blood from the cortex to the medulla. Should this theory be accepted the problem of what causes the peripheral vascular failure producing the anoxia still remains unsolved.

The treatment of blackwater fever has been modified in certain important respects during recent years. It is now realized that the intensive alkali medication based on the mechanical blockage theory of Baker and Dodds and formerly widely used is not suitable for all cases and may indeed do harm.[30] Moreover, it has been shown that acidosis, formerly considered a characteristic feature of blackwater fever, is by no means invariably present in that condition.[31] Again, dehydration calls for free administration of fluids, but intake must be carefully balanced against output, since oedema and waterlogging can easily occur.[32] Intravenous plasma followed by intravenous saline alternated with isotonic glucose is the treatment for vascular failure. Blood transfusion is indicated if the red cells fall to 1,500,000 per c.mm., or if the lysis of cells is proceeding very fast. In such circumstances it is essential that the donor's cells and the patient's serum be cross-matched. A full-course treatment with an antimalarial drug (other than quinine or pamaquin) should be given when malaria parasites are demonstrable in the peripheral blood. One of the most important therapeutic measures is the protection of the patient from any form of movement or exertion. This is well illustrated by the old African adage, "If you find a person with blackwater, build a *banda* (grass hut) over him," and is the basis of the barbiturate medication advocated by Burkitt.[33]

A review of the vast volume of literature about blackwater fever leaves the reader with the impression that almost all the known facts about its nature, aetiology, and prophylaxis were established or confirmed by Stephens and Christophers as the result of their researches in Central Africa at the beginning of the century.[16] They showed that blackwater fever was brought about by exposure to severe and long-continued malarial infection, which induces a condition of unstable equilibrium in the blood before quinine or any other determining factor can precipitate an attack, and that the type of malaria most frequently associated with this condition was malignant tertian. They deduced from these findings that the best way to prevent the disease was to institute vigorous malaria control measures. The occurrence of blackwater fever is one of the cardinal signs of malarial hyperendemicity, and denotes that infection is not only intense and frequent but that conditions favouring the transmission of the disease exist throughout the greater part of the year. Conversely, the disappearance of blackwater fever is one of the earliest indications of successful control of malaria in such areas. Non-immune immigrants are the most frequent victims of blackwater fever, which, though not unknown, is comparatively rare among indigenous populations of malarious areas. Stephens[34] compiled a list of 218 cases with 73 deaths recorded among negroes in various African territories over periods of 10 or more years. Leclef[35] cited 11 cases occurring within six months among Africans employed in certain copper mines in the Belgian Congo, and 17 additional cases with three deaths were recorded in the same labour force in the following year.[36] Giglioli,[37] in British Guiana, noted that, though blackwater fever was rare among Africans, the cases which did occur were if anything more severe than in members of other races. The syndrome was three times as prevalent among children as in adults, a finding in harmony with the generally recognized view that its incidence is very largely dependent on the presence or absence of malarial immunity.

In a recent issue of this *Journal* Jelliffe[38] reported four cases of blackwater fever among African children treated at Ibadan, Nigeria; in three of these there was a history of occasional dosage with quinine during early childhood. In Nigeria severe and often fatal pernicious attacks of subtertian malaria are seen comparatively frequently in young African children and appear to represent the price paid for the development of malarial immunity in the surviving majority.

[20] Foy, H., and Kondi, A., *Trans. roy. Soc. trop. Med. Hyg.*, 1943, **37**, 1.
[21] Christophers, S. R., and Bentley, C. A., *Scl. Mem. Off. med. san. Dept. Govt. of India*, 1908, No. 35.
[22] *Trans. roy. Soc. trop. Med. Hyg.*, 1934, **28**, 141, 307.
[23] Butts, D. C. A., *Amer. J. trop. Med.*, 1945, **25**, 417.
[24] Manson-Bahr, P. H., *Manson's Tropical Diseases*, 1929, London.
[25] Blacklock, D. B., and Macdonald, G., *British Medical Journal*, 1928, **2**, 145.
[26] Wenyon, C. M., *Protozoology*, 1926, London.
[27] *Arch. Schiffs- u. Tropenhyg.*, 1920, **24**, 329.
[28] *Brit. J. exp. Path.*, 1925, **6**, 247.
[29] *Lancet*, 1944, **2**, 403.
[30] Maegraith, B. G., and Havard, R. E., *Lancet*, 1944, **2**, 338.
[31] —— *Trop. Dis. Bull.*, 1946, **43**, 801.
[32] —— *Lancet*, 1945, **2**, 58.
[33] *British Medical Journal*, 1943, **1**, 737.
[34] *Blackwater Fever*, 1937, London.
[35] *Ann. Soc. belge Méd. trop.*, 1931, **11**, 293.
[36] de Decker, ibid., 1932, **12**, 213.
[37] *Trans. roy. Soc. trop. Med. Hyg.*, 1932, **26**, 204.
[38] *British Medical Journal*, 1951, **1**, 1117.
[39] Findlay, G. M., *Ann. trop. Med. Parasit.*, 1949, **43**, 213.
[40] *Malaria Conference in Equatorial Africa*, 1951, World Hlth Org. techn. Rep. Ser., No. 38, Geneva.

There has been a marked reduction in the incidence of blackwater fever among Europeans in Nigeria in recent years, probably because of the regular drug prophylaxis now adopted almost universally. On the other hand, an increased incidence has been reported in African troops, who, though not on drug prophylaxis, were partially protected from malarial infection by other measures during the war years.[39] Jelliffe fears that the casual use of antimalarial drugs in the households of educated Africans may result in an increased incidence of blackwater fever, particularly among young children, who will neither be adequately protected against malarial infection nor be able to build up an effective immunity. He suggests that only the more intelligent mothers be advised to give their children chemoprophylaxis, in case its regular administration into adult life might not be continued.

In the long run the elimination of blackwater fever from a community must depend primarily on the application of modern methods of malaria control in all malarious areas (irrespective of the degree of endemicity), as recommended by the Malaria Conference in Equatorial Africa[40] recently held in Kampala under the auspices of the World Health Organization. An essential preliminary is the establishment on a permanent basis of an effective antimalaria organization with the least possible delay.

INFANTILE CEREBRAL PALSY

Though Collier[1] argued persuasively that all cases of infantile cerebral palsy were due to a primary neuronal degeneration, it is generally agreed that this is only one of the causes and that the condition may also be the result of birth trauma, or prolonged neonatal asphyxia, or of acute cerebral disease occurring during the first year or so of life. Stewart[2] found no evidence of uniform abnormality in a pathological study of 50 cases in which cerebral diplegia was associated with mental deficiency, and concluded that it was most unlikely that all cases were due to the same cause; he also felt that birth injury had been over-emphasized in the aetiology. Asher and Schonell[3] have carefully inquired into the history of 400 patients with infantile cerebral palsy in the Birmingham district, including those in mental deficiency institutions and in special schools. They personally examined each patient and came to the conclusion that 51 were suffering from a post-natal cerebral lesion. In classifying the neurological disturbance in the 349 congenital cases they have avoided the common term diplegia, using instead quadriplegia and paraplegia, without, however, implying that a spinal abnormality was present—a significance sometimes given to these terms by neurologists. In 290 patients (83%) the disability was essentially a spastic paralysis (hemiplegia in 102, paraplegia in 90, symmetrical quadriplegia in 77, and asymmetrical quadriplegia in 18). There were 36 athetoid patients, and 17 had a combination of spasticity and athetosis. The few remaining patients suffered from cerebellar ataxia.

There was better indication of the possible aetiology in the athetoid cases than in the larger spastic group. The incidence of abnormal labour and birth injury among the athetoids was significantly greater than that for the whole series, and in 12 of them there was a history of severe neonatal jaundice. Rhesus tests were carried out in five of these and gave no indication of ordinary Rh incompatibility; of the remaining seven, four were first-born, and in only one of the other three was there any suggestion from the history of Rh iso-immunization. The authors suggest from these findings that congenital athetosis is usually the result of birth injury, asphyxia, or of neonatal jaundice, whether or not due to Rh iso-immunization. The findings in the cases of spastic paralysis were less definite, and Asher and Schonnell think that birth injury may be the cause in some cases while others are the result of unknown genetic or intrauterine factors. They found no evidence that asymmetrical spastic paralysis was more likely to be due to birth injury than was symmetrical paralysis.

The findings in the 51 patients with post-natal cerebral paralysis were interesting. In 19 athetosis followed icterus gravis neonatorum, in which the serology and family history were typical of haemolytic disease of the newborn; but the clinical condition in these patients did not differ from the other athetoid cases in the series, and there was no evident relation between the severity of jaundice and the degree of neurological disability. In nine cases for certain, and probably in two others, cerebral palsy occurred after meningitis in infancy; and two patients developed sudden hemiplegia during acute infections—in one case measles and in the other diphtheria. Twelve children with hemiplegia had had a fit or a series of fits during the first or second year of life: in 11 of these the disability was greatest at the onset and gradually improved. These were examples of the "acute infantile hemiplegia" which has been much discussed[4]; it is probably vascular rather than infective in origin.

1 *Brain*, 1924, **47**, 1.
2 *Proc. roy. Soc. Med.*, 1942, **36**, 25.
3 *Arch. Dis. Childh.*, 1950, **25**, 360.
4 Wyllie, W. G., *Proc. roy. Soc. Med*, 1948, **41**, 459.
5 *Arch. Dis. Childh.*, 1950, **25**, 325.

Craig[5] has considered a different aspect of the problem. He kept under observation 593 infants whom he had personally examined within two days of birth and in whom there were symptoms and signs of intracranial irritation. The diagnosis was made on clinical grounds, and no lumbar punctures were performed, since he felt that they would give no useful information and were therefore not in the child's interest. The follow-up period varied from a year up to five or more years in 306 of the patients. There was physical or mental disability either separately or together in 52 children. In 41 neurological involvement was evident: 17 had a spastic hemiplegia, eight a monoplegia, five bilateral asymmetrical paralysis, two spastic diplegia, five ataxia and athetosis, and four hydrocephalus. Craig concludes that evidence of intracranial irritation in the neonatal period offers no reliable indication of the likelihood of permanent sequelae developing, with the possible exception of infants in whom severe intracranial haemorrhage is suspected. His findings also suggest that it is a rare exception rather than the rule for permanent sequelae to develop in infants who survive post-natal intracranial irritation and in whom there are no signs of residual disability during the neonatal period.

These two investigations help to disprove the rather prevalent idea that birth injury is the most important cause of congenital cerebral palsy. There seems little doubt that some developmental influence is often to blame, but it is still impossible to say whether this interference with the normal development of the foetal brain is or is not genetic in origin.

PSITTACOSIS IN THE FAROE ISLANDS

Last October the University of Copenhagen conferred the degree of Doctor of Medicine, honoris causa, on Dr. R. K. Rasmussen, who has spent practically all his professional life as a general practitioner in the Faroe Islands. Behind this rare honour there is, of course, a story. When, at the age of 33, Rasmussen left Denmark to spend the next 30 years in the Faroe Islands, a dependency of Denmark, his friends thought he was throwing great talents away. But soon a series of epidemiological studies began to stream back from the islands to Copenhagen, where they were duly published. These studies were concerned with acute epidemic myalgia, tuberculosis, whooping-cough, blindness, and various other ailments.

In 1930 a Danish colleague, Dr. A. A. Vaag, also working in the Faroe Islands, observed five cases of a febrile disease which he called primary epidemic alveolar pneumonia. In September, 1933, he observed 26 similar cases, an account of which he published in 1934. All the patients were adults, and 90% of them were women. The fatality rate was high for pregnant women. Browsing over this and other publications on the subject, Rasmussen was struck by the similarity of these cases to the cases of psittacosis about which he had read. He scrutinized the history of all the epidemics of the former disease observed in the Faroe Islands during the period 1934–7, and he came to the conclusion that the fulmar, *Fulmarus glacialis*, might possibly be the vector of this disease. The fledglings of this bird are caught before they can fly by the islanders, and are counted as a delicacy by them. In Morris's *History of British Birds* Pennant wrote: "No bird is of such use to the islanders as this: the fulmar supplies them with oil for their lamps, down for their beds, a delicacy for their tables, a balm for their wounds, and a medicine for their distempers."

To check his hypothesis Rasmussen secured the co-operation of his colleagues in the islands, getting them to collect dead specimens of the fulmar, and to take samples of blood from patients suffering from primary epidemic alveolar pneumonia and various tissues from those who had died of this disease. The specimens were kept on ice till they could be put in cold storage on board a ship carrying them to Copenhagen. Here the health authorities and State Serum Institute took charge of them and dispatched them by aeroplane to London and Berlin. In London Professor Bedson carried out complement-fixation tests on the serum of three patients with the virus of psittacosis, and in Berlin, at the Robert Koch Institute, Haagen and Mauer extracted the virus from the organs of young fulmars, provoking in mice reactions characteristic of psittacosis virus reactions. The virus they found possessed the morphological and staining features of the psittacosis virus. Some of the parrots infected with the virus developed psittacosis. The same virus was isolated from the blood of a woman suffering from primary epidemic alveolar pneumonia, and when she died of this disease the virus was cultivated from her organs.

Haagen and Mauer, at a meeting of the Berliner Mikrobiologische Gesellschaft in 1938, presented a paper on their bacteriological investigations, and Professor Thorvald Madsen, of the State Serum Institute in Copenhagen, followed with an account of the steps leading up to the discovery. A full account was published later.[1] As a masterpiece of cleverly co-ordinated research, this achievement stands out as a remarkable tribute to a rural general practitioner who, without first-hand contact with the clinical side of the problem to begin with, and without the technical equipment of a modern laboratory, set his imagination to work and picked up one clue after another till he was able to build up a plausible case for a hypothesis which led to a dramatic discovery.

[1] *Zbl. Bakt.(1 Abt. Orig.)*, 1938, **143**, 81, 89.

PENICILLIN IN THE LUNG

It is now a commonplace that systemic administration of penicillin is a very effective treatment for acute bacterial pneumonia. In chronic pulmonary infections, however, such as chronic bronchitis, bronchiectasis, or

lung abscess, systemic penicillin has never proved particularly effective, even when the organisms involved could be proved to be sensitive to the drug. One reason for this difference probably lies in the fact that, whereas during systemic administration of quite small doses of penicillin to patients with acute pneumonias the drug can regularly be detected in the sputum in concentrations of 0.04 unit per ml. and upwards,[1] it is usually absent, or present only in very small amounts, in sputum from patients with chronic types of infection. Presumably in the acute cases, with considerable parenchymatous involvement, the sputum consists partly of a passive transudate from the pulmonary capillaries, and its penicillin content reflects that of the blood stream. In the case of chronic infections, however, most of the infectious process occurs in bronchi or in epithelized cavities, the lining cells of which constitute an effective barrier from the blood stream. Most of the sputum is actively secreted, and there is no particular reason why penicillin should be secreted in it. These facts provide a rationale for the widespread administration of penicillin by inhalation as an aerosol.

A report has recently appeared[2] of a small trial in this country of a new ester of penicillin (benzylpenicillin diethylaminoethyl ester hydroiodide) which, on systemic administration, appears to be concentrated in the lungs in experimental animals and to be secreted in the sputum of patients with chronic pulmonary infections. The ester was originally developed by Professor K. A. Jensen and his colleagues[3] in Denmark as a depot penicillin. As such it was not superior to procaine penicillin, but investigation of its distribution in the body showed a concentration in the lung several times greater than in other organs and even higher than the blood level. Clinical trials have borne out these findings. The therapeutic results in chronic pulmonary infections cannot really be assessed on data at present available, but there seems to be a marked reduction in volume of sputum, with a tendency for Gram-positive organisms to decrease and possibly be replaced by *Bact. coli* type. Such results resemble those obtained by inhalation treatment. As Humphrey and Joules remarked about inhalation:

"It is difficult to say yet whether any permanent improvement is likely to be effected by continued or repeated treatment of long-standing cases of chronic bronchitis with emphysema or of bronchiectasis. The persistence of mucoid sputum is bound up with the structure of the chronically inflamed bronchi and bronchioles. They are usually lined with a complete epithelium, and the walls contain numerous mucin-secreting glands. Beneath the epithelium is a layer, more or less thick, of fibrous tissue which is highly vascular and infiltrated chiefly with plasma cells and lymphocytes. It would be very optimistic to suppose that such glands will regress, or that an epithelized cavity will alter much, even though pyogenic infection be permanently staved off and no further fibrosis take place."

[1] Humphrey, J. H., and Joules, H., *Lancet*, 1946, **2**, 221.
[2] Heathcote, A. G. S., and Nassau, E., *ibid.*, 1951, **1**, 1255.
[3] Jensen, K. A., Dragsted, P. J., and Klaer, I., *Ugeskr. Læg.*, 1950, **112**, 1075.

SOCIAL WORK IN MENTAL HEALTH

The National Health Service Act has demonstrated the need for extending non-medical services of many kinds in order to leave doctors free for clinical work, and the demand for some medical auxiliaries has far exceeded the supply of those leaving the training schools. In the mental health service, for instance, there is an acute shortage of trained social workers. There are only 331 psychiatric social workers in active practice, and even these are erratically distributed, most being in the south of England. A committee which was set up by the Minister of Health three years ago, with Professor J. M. Mackintosh as its chairman, to consider the training, qualifications, and employment of social workers in the mental health service has just issued its report.[1]

Of psychiatric social workers the committee says, "Their professional status stands high," and it estimates that more than 1,500 are needed, together with a still larger number of trained and experienced mental welfare workers. It believes that a sound, well-balanced course of social science is an indispensable foundation for the practice of social work in the mental health services, and it recommends that those wishing to enter this profession should be offered a general training, linking the academic and the practical, at university level and designed to meet the needs of social workers engaged in case work. Psychology should be taught in its application to the living situations which the candidate is likely to meet in her daily experience. As there are no standardized courses of training for mental health workers (other than psychiatric social workers) the committee recommends that appropriate courses should be organized as soon as possible. These should include "in-service" training—which American experience has shown to be most valuable educationally—for those already holding appointments under a local authority. There should also be instruction in the medical, social, and legal aspects of mental health work, as well as visits to mental hospitals and clinics. New entrants to the local authority service should spend at least six months under the supervision of an experienced worker, and then, if found personally suitable, should have "in-service" training for two years. With a view to attracting recruits immediately to the general mental health services a trainee system on a regional basis is recommended. It would be most suitably handled by the regional hospital boards, which are based on university centres and are also in a position to work closely with local health authorities. The committee thinks that the designation "psychiatric social worker" should be restricted to persons holding a university mental health certificate, and that a register of them should be kept. It also urges economy in the use of their services. They should not, for example, be given clerical duties, but the fullest use should be made of their time and skill for the social work for which they have been trained.

[1] Report of the Committee on Social Workers in the Mental Health Services, 1951, H.M.S.O., London.

HYDRAMNIOS

Several maternal and foetal disorders are commonly associated with hydramnios, and almost certainly different causes operate in different groups of cases. The use of radioactive substances in research has not yet solved the problem of aetiology, but they have shown that the liquor amnii is far from a stagnant collection of fluid, for its water content is entirely replaced about every three hours.[1] It is commonly stated that cardiac and renal disease can cause hydramnios, but diabetes mellitus is the only general maternal disease of particular aetiological importance. Peel and Oakley[2] found hydramnios in about 30% of pregnancies in diabetic women, but the reason for the association eluded them. In particular they found no relation between the amount of liquor and either its sugar content or the mean maternal blood sugar during pregnancy. In their own 141 cases foetal death occurred in 25% and congenital malformations in 6.3%.

When hydramnios occurs in the absence of maternal diabetes the prognosis for the foetus is much worse. Macafee[3] recently reported a series of 147 pregnancies, single and multiple, with hydramnios. Only six of the mothers were diabetics, and the total foetal loss was 55.5%. He found a gross foetal abnormality demonstrated by *x* rays in 54 of the pregnancies, by far the commonest malformation being anencephaly, which as usual occurred predominantly in female foetuses. Hydrocephalus is rarely associated with hydramnios except in pregnant diabetics. But even when no malformation is seen radiologically the outlook for the foetus is still clouded, for Macafee found that in 20% of such cases some abnormality was apparent at or after delivery, and the foetal mortality in this group was 33%. Radiological examination is therefore advisable in every case in which the clinician finds more liquor present than is usual for the stage of pregnancy. Not only may a malformation be thus demonstrated, but a multiple pregnancy will be diagnosed in about 15% of cases.

The treatment of hydramnios when the foetus shows no abnormality radiologically but the symptoms demand active intervention some weeks before term has been the subject of controversy. In the acute cases Rivett[4] advocated abdominal paracentesis, a procedure first reported by Henkel[5] in 1919, but Macafee doubts its value. Occasionally the excess of fluid does not reaccumulate, sometimes because one foetus in a multiple pregnancy has died following the operation. In chronic cases treatment is never so urgently required, and putting the patient to bed may bring about improvement. Abrams and Abrams[6] recommended the administration of large doses of ammonium chloride, but their claims of success have not been confirmed. In either acute or chronic cases the aspiration of liquor through the abdominal wall, though open to many theoretical objections, is in practice a safe procedure—the repeated withdrawal of smaller amounts being preferable to the removal of a large quantity of liquor. Where the only alternative is the rupture of the membranes vaginally, with the certainty that the onset of labour will be precipitated, nothing will be lost by abdominal paracentesis, while there may be gained for the premature foetus a respite which will enable it eventually to face labour and neonatal life with better prospect of survival.

1 Vosburgh, G. S., Flexner, L. B., Cowie, D. B., Hellman, L. M., Proctor, N. K., and Wilde, W. S., *Amer. J. Obstet. Gynec.*, 1948, **56**, 1156.
2 *Trans. XIIth Brit. Cong. Obstet. Gynaec.*, 1949, London, p. 161.
3 *J. Obstet. Gynaec., Brit. Emp.*, 1950, **57**, 171.
4 *Amer. J. Obstet. Gynec.*, 1946, **52**, 890.
5 *Zbl. Gynäk.*, 1919, **43**, 841.
6 *Amer. J. Obstet. Gynec.*, 1946, **52**, 790.

ESTABLISHMENT OF REGISTRARS

The proposal[1] last November to reduce drastically the number of registrars aroused such strong feelings in all sections of the medical profession that within a few weeks the Ministry wisely agreed to the publication of a statement[2] which went some way to allay the anxieties of registrars and of the hospitals employing them. The report of the Joint Committee in this week's *Supplement* (page 47) describes the progress of the discussions which have since taken place. The most important change which the Ministry has made in the original proposals is to lengthen the period of training of senior registrars from three to four years (or longer in the case of some specialties). The effect of this is to raise the suggested establishment of 600 senior registrars for England and Wales to 960 (the provisional establishments for Scotland have already been reported[3]). It is believed that the total number of senior registrars is something over 1,500, of whom between 500 and 600 are in their third year of training. The Joint Committee considers that "a large majority" of these third-year registrars will be able to obtain consultant posts or a fourth year of training. Those no longer kept on the training establishment will be able to retain their appointments temporarily if they are still needed for the work of the hospitals. The number of senior registrars in the first or second year of training will still be much in excess of the proposed establishment—an establishment which obviously must bear some relation to consultant vacancies—but the extension of the training period will enable more of them than at first seemed likely to enter the second, third, or fourth year of training.

The Ministry's ill-considered circular showed a failure to realize that a reduction in the establishment of senior registrars and registrars would leave many hospitals without enough doctors to carry on the day-to-day work. It has now been agreed that regional boards and boards of governors will, for the time being, fix their own establishments of registrars in accordance with the needs of hospitals. The Joint Committee has pointed out that young doctors working as registrars gain valuable experience for general practice and other fields of medicine, and that this grade should not necessarily be regarded as a training grade for potential consultants. The corollary of this would seem to be that the prospects for ex-registrars in general practice will have to be improved.

1 *British Medical Journal*, 1950, **2**, 1158, and *Supplement*, 1950, **2**, 204.
2 Ibid., *Supplement*, 1951, **1**, 24.
3 Ibid., *Supplement*, 1951, **1**, 251.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE NERVOUS CHILD

BY

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Under the 1944 Education Act every local authority is empowered to provide help for the maladjusted child. This may take the form of a special school, either day or, more usually, residential, or special classes within an ordinary school. Just as clinics are provided for sight and hearing disorders, so clinics are provided for the treatment of the maladjusted child. Further, a department of psychiatry is now the rule rather than the exception in the general and teaching hospitals, so that a number of clinics dealing with the problems of the nervous child have also been set up by the regional hospital boards. As, however, it is estimated that 1 to 1.5% of all children will require some psychological help, it is quite obvious that even the growing number of child-guidance clinics and trained workers in child psychiatry will be inadequate to meet these requirements. The family doctor is therefore no stop-gap substitute for the fully staffed child-guidance clinic. He is in many cases the front line of the attack on childhood neurosis, and is in a good position to carry it, for he probably knows the home setting and will have watched the situation as it developed. Who is better able to assess the contributions, for or against, made by the grandparents, or the schoolteacher, or the next-door neighbours?

Methods of Approach

Because the teaching of child psychiatry can hardly be said to have existed in the curriculum of the pre-1939 medical student, there is still a tendency for doctors to regard the more severe behaviour problems of children as something which only an expert can touch, or to swing to the opposite extreme and imply that a touch of common sense, or forbearance, or the rod, depending on the particular school of thought, would have prevented all this happening, thus adding very materially to the harassed parents' feelings of inadequacy. Whatever the problem, it is unlikely to be solved by any psychological sleight of hand, and therefore nothing can replace in clinical importance the taking of a good history. Supplied with that, the doctor may succeed in giving some much-needed reassurance or caution. This should be based on understanding rather than direct advice or prohibition.

History-taking

The busy surgery is a bad place for history-taking: very often both mother and child are present, time presses, and the whole clinical picture is built up on a false premise. Nine-year-old John is wetting his bed. Perhaps his mother connects it with her brother's early death from nephritis. It may be a long journey to arrive at the fact that John is a dull boy who is being too hard pressed at school and challenged by his quicker younger sister.

In the long run (and therefore as soon as possible) it will save time to spend time on taking the history in a situation of privacy and away from the child. One thirty-minute talk will uncover more of the truth than three ten-minute talks. Any psychiatric history must take the physician behind the defence lines, as any child's problem will in some measure be a family problem restated. Indeed, the art of history-taking lies not so much in leaving no stone unturned as in creating an informal situation in which a troubled parent will feel free enough to admit to herself, and to the doctor, something of what is worrying her. Premature reassurance will not stop her worrying, but it may discourage her from telling the rest of her story. Hence the fewer questions asked the better; those which are asked should serve to direct the course of the story rather than to elicit the facts. The actual words used can sometimes be noted: they are often revealing. Of John the bed-wetter's sister it was said, "Oh, Mary, she's a different child altogether, a joy from the first go." Such a remark may hint at family attitudes which may be of the highest relevance.

In obtaining a history of the developmental milestones the family doctor may know only too well that this child has always deviated from the average, but he may succeed in uncovering attitudes and feelings within the family setting rather than facts and figures as such. While the purpose of a history is to record information, the taking of it plays an important part in establishing a relationship and an entry into the tensions which are contained in any family.

Examining the Child

Children who are taken to the doctor have many odd ideas about it, and their previous experiences will determine whether they view it with fear or dislike. It is just as important to try to make some contact with the child as it is to get behind the parents' defences. Most children will use paper and pencil if given the opportunity and will often tell the physician a good deal about themselves in the pictures they make while waiting outside. A small girl, very jealous of her sister, drew a house. When asked to draw the people who lived in it, she added a mother and a father and a third figure. Asked about it, she said, "It's a boy; they have only *one* child" (very far removed from her own situation). This made a good opening for her to talk about the way she felt in relation to the baby sister. Active play, however simple, is always more revealing than books or games of the puzzle variety, and a history taken at home with the child at play in an adjoining room can reveal a good deal of the situation. It may be, however, that knowledge of the "nervousness" has been gained in helping the child through some physical illness.

However much a counsel of perfection, if the family doctor is to attempt any kind of alleviating treatment some time *must* be given to the mother alone, and wherever possible the father, too, should be brought into the picture. Time spent alone with the child is equally important, although the child will not be able to develop his contact so quickly. Even where outside help is

available, in a clinic or a residential school, work on these lines will be valuable to both patient and doctor.

This all takes less time than the more usual procedure of remedies and pointless investigations, at the end of which the parents are told that *as everything is negative* the problem must be psychological. This is always a disappointing diagnosis to have made on negative findings only, and an unconvincing one when arrived at after unsuccessful treatment. The psychiatric diagnosis, as any other, should be built up on positive findings, which may be confirmed by excluding organic possibilities as the final step.

Important Aetiological Factors

Approached in this way even a complex family situation will begin to declare something of the way in which it has come about. The idea with which the child was conceived—for example, to procure the mother's discharge from the Services—the circumstances of his birth and early nurture, these tell their own story. In hearing about his behaviour and his responses in babyhood, much will be learned of parental attitudes, and in the first year of life probably nothing is so important as the child being able to receive love and affection and a continuity of handling.

Separation in Early Life

Evidence is accruing that prolonged (say, upwards of two to three weeks) separation from the mother predisposes the child to a mourning reaction which may eventually result in what is tantamount to an emotional atrophy.* Not only is the child often ill but he fails to develop either his intellectual powers or his normal degree of emotional maturity. Eventually such children become indifferent. They appear to owe allegiance to no one. They are quiet and withdrawn, sometimes aloof, often easily led, and have a sustained sense of reproachful hostility This can sometimes be seen as a definite negativism and lack of co-operation, as for instance in stealing, and sometimes as a more projected reaction of hostility based on a sense of persecution. The child feels unloved, however much is done to "make up" for his earlier loss by separation.

Position in the Family

This often has a bearing and is always worth noting carefully. The eldest child has a mother who is inexperienced and apt to take everything too seriously. He is the only one to be an only one, even if temporarily so. Similarly the youngest stays the baby and is never succeeded, while the middle of three has often to establish himself against bilateral competition. There are difficulties, too, inherent in the position of the only girl in a family of boys and vice versa. Grandparents are apt to establish favourites more readily than parents, and one child may have a particular handicap which singles him out for attention.

Physical Disabilities

Intercurrent illness has its own bearing, as it may make an already anxious parent still more inclined to over-react, or it may induce a feeling of irritation and frustration towards a child who is repeatedly ill. Enuresis in one child becomes a very real family problem when it prevents the whole family from taking a summer holiday.

In a general way, a child who has a physical illness is easier for the parents to accept than one with a psychological illness, hence perhaps the desire to find physical causes for what are really emotional ills. Where a child is seriously handicapped care will be needed to prevent a psychological overlay, associated with the period of abnormal living and with loss of schooling, reactions of siblings and others, and the real anxiety of being ill. The supposed "gain" in illness is more often an inability to dispense with the special props which have been temporarily necessary, and time is needed to regain confidence.

Stresses Outside the Home

It sometimes becomes clear that the child's difficulties have more to do with school than home. Many nervous children dread school and cannot tolerate the mild degree of "baiting" which is likely to come their way. This is perhaps more likely in only children and in those from small families who spend their time in carefully restricted lives mainly spent with adults.

Sometimes the school is at fault, but more often unhappiness at school is associated with all-round backwardness which has not been discovered in a large class, or with some degree of educational retardation associated with average ability but poor achievement. This is especially true of the child who has missed school through illness and long convalescence. While the history may point the way to this diagnosis, it will be clarified only by an intelligence test done under leisured conditions. Tests done in a group in class are particularly apt to be misleading in the case of educational retardation, for they are apt to fail in bringing out the latent ability.

Treatment by the Family Doctor

When these and other factors have been assessed, how far is the family doctor helped in deciding whether to send a case to a clinic or treat it himself? As has been implied, the decision may be forced on him by having no alternative to offer. He will still want to evaluate the task with which he is faced. If he has an alternative, such evaluation is even more important. Certain factors will help greatly in making the doctor decide that home treatment is feasible.

Stable Family Background

Of these, none is more important than a stable united family, interested in and aware of the problem in their midst, anxious to help, and not unduly perturbed by it. The expression "anxious to help" needs closely defining, because such an attitude must include a willingness to undertake the responsibility of helping, and indeed a willingness sometimes to tolerate the symptom continuing. There are occasions when such remarks as, "I leave it entirely in your hands, doctor," indicate a demand to be relieved of any further contact with the problem. The over-anxious mother who cannot bear her child to vomit may unconsciously foster the need for attention, as well as choice of this particular symptom.

Anyone attempting to carry out treatment in a family will find himself steering this difficult course between the parents' guilty feeling of responsibility for a problem child and their natural antipathy to having their own lives put out by it. In other words, they tend to be angry with themselves or angry with the child, knowing that either attitude is probably indefensible.

**Maternal Care and Mental Health*, by J. Bowlby. W.H.O. Monograph Series. No. 2. Price 10s. 1951.

Thus, an important part of the doctor's role is to be an Aunt Sally for either side, relieving both parents and children of some of the sense of failure, and accepting on their behalf some of the resentment. In this connexion one wonders whether children do enjoy their own bad behaviour. It seems clear that as a rule they are in trouble with it from the start. The resulting ostracism, whether at home or at school, is undoubtedly a source of much neurotic human suffering.

Limited Crises

When there is evidence that the disturbance is a passing phase, particularly when it occurs as a reaction to some environmental change, there is every reason for the family doctor to take the situation in hand and tide over the crisis. Children tend to over-react to changes, whether in people or in their surroundings. If this is understood and allowed for, many of these reactive problems can be quickly solved, as they doubtless have been for hundreds of years by the parents of a more leisured age.

Differing Standards

The extent to which a problem is localized is also of some diagnostic significance. The child who is no trouble at home but always in difficulty at school may need some quite simple step in adjustment. It may be that standards vary greatly in the two places, but often the localized problem proves to be a generalized one which becomes manifest in the less tolerant environment. At least, such a situation deserves carefully exploring to see whether the child really lives part of his life in a perfectly satisfactory way, and if so whether there is something seriously wrong, apart from himself, in the other place where he seems always to run into trouble.

The Difficult Years

Finally, there is the problem arising at an age when problems are rife. In the pre-school stage, named by Susan Isaacs "the period of normal negativism," a child who is fighting out his first battles with his much-loved parents, bewildered at finding himself on the wrong side, so to speak, will quite certainly produce much problem behaviour. Even in quite small children such problems may be very severe.

June, aged 3 years 4 months, reacted severely to her father's period of service abroad. She had a younger sister, aged 8 months. June woke screaming once or twice between 10 p.m. and midnight. Later in the night she would cry ceaselessly and her mother would be unable to leave her, often for some hours. This had begun within a few days of father leaving home; the single-handed mother had had only a few hours' sleep nightly for two months when first seen.

George, aged 19 months, had been clean as a baby, but relapsed into severe negativism over pot-training. He soiled himself daily for some months, and then would defaecate in one particular corner of the kitchen, and only if his mother was out of the room. Re-education to normal habits took upwards of one year.

Difficulties such as these try the patience, and so afford opportunities for an expression of exasperation or despair which may form the corner-stone of a more serious neurosis in the child's later life. The need for prompt care in handling these problems is mainly in order that they should not become a focus for bad feeling. Whether a child defaecates in his trousers, in the coal-bucket, or in his pot is of little importance compared with the way he and his family feel about him doing so. The advice that "he will grow out of it" is, by itself, never enough to allay the feeling of despair which sometimes accompanies the problems posed at this notoriously difficult age. What makes them rewarding cases to treat is the fact that often quite a short time spent in understanding the feelings of both parents and children of this age goes far to reduce tension and, by so doing, to relieve the symptoms.

Contraindications to Home Treatment

If these are the points which may lead the general practitioner to try his hand, he may be wise not to undertake a case in which the child's family is divided against itself, or in which the material circumstances in the home—for example, overcrowding—hardly allow of a normal adjustment. The same warning applies to the very long-standing case in which every part of the child's life is affected by his maladjustment. The older the child, apart from those instances of an isolated reactive problem, the more likely it is that other and deeper factors lie behind an apparently sudden inability to conform. He will, however, even in the case of the older child, take a good look round to see whether the need for conformity is there, or the demand for it unreasonably pressing.

Simple Methods of Treatment

Are there any simple methods of treatment? I wonder how many psychiatrists would care to pass judgment on exactly what has brought about a cure in any given case. Is it good medicine to suggest that a simple remedy should always be tried first? Here, again, the keyword is good diagnosis, and a good diagnosis depends neither on flair nor on training so much as on good relationships and a good history. It might be reasonable here to illustrate from a physical analogy. Most of us would agree that to prescribe a tonic and a holiday for someone with early pulmonary tuberculosis before diagnosing the condition would be a dangerous waste of time. But most of us have discovered unsuspected healed foci of tuberculosis which have presumably responded favourably to just this kind of regime. In the psychiatric treatment of children, it is almost impossible to avoid this danger, for it is so often necessary to revise the diagnosis from time to time in the light of new information becoming manifest during treatment.

The role of the family doctor is therefore likely to be twofold. He will be called in early to advise on the first stages of a problem, and he may from time to time be in a position to forestall a problem by his handling of intercurrent illness or upset.

At all times the doctor must be on his guard against inadvertently causing a psychiatric problem himself. It is quite common to meet with children who are kept off exercise for years for supposed chorea, and a child is often made afraid of school by having missed an essential stage and so fallen behind. If the child then begins to have nightmares, or to go off his food, frequently we find that "three months' convalescence" is recommended without any reference to how these symptoms have arisen. Would we send our own children away for a term so light-heartedly?

Conclusion

In treating nervous children the doctor needs time to gain his facts. It will repay him to study feelings and family attitudes rather than actions, and he may well

find that the patient's or the parents' own words will tell him more than his own questions. His conclusions will be strengthened by his intimate knowledge of the background in which his child patient lives.

He should be careful to avoid creating physical anxiety because there seems no obvious explanation for a mental symptom, and he should seek to judge fairly between mental and physical suffering without letting the patient play one off against the other.

He may need to remind himself that if the child could "pull himself together" he probably would. A child does not enjoy the scenes he creates; indeed, he is often panic-stricken by them.

If the doctor decides to reassure a mother, it will be because he can feel sure that a symptom is not dangerous. He would be unwise to dub it unreal or imaginary on that account. He may do a lot, in a stable family, to restore mutual confidence. He can comfort the inexperienced mother with the knowledge that it takes most of the threescore years and ten to learn how to live, and that one function of family life is to provide a warm shelter where a child can safely display his deepest fears, knowing that they will be understood and cared for.

INTERNATIONAL CONGRESS OF CLINICAL PATHOLOGY

The Minister of Health, Mr. Hilary Marquand, opened the International Congress of Clinical Pathology at Friends House, Euston Road, London, N.W.1, on Monday, July 16. He was supported on the platform by his Chief Medical Officer, Sir John Charles, and the Adviser in Pathology, Professor S. P. Bedson, the President of the British Association of Clinical Pathologists, Sir Lionel Whitby, together with the officers of the International Society of Clinical Pathology and the chairman and secretary of the executive committee of the Congress. The Minister, who referred in his speech to the prime importance of adequate laboratory facilities both for hospital services and also for general practitioners, was thanked by Professor Robert Cruickshank (London) and Professor Tullia de Sanctis Monaldi (Rome).

The President of the International Society, Dr. S. C. Dyke, then presented to the Minister the vice-presidents of the Congress nominated by the Member Societies: Australia, Dr. Edgar Thomson; Belgium, Dr. D. Jaumain; Cuba, Dr. Antonio Sellek; France, Professor M. Polonowski; Great Britain, Dr. J. G. Greenfield; Italy, Professor Tullia de Sanctis Monaldi; Spain, Dr. D. Antonio Utrilla Dominguez; Turkey, Professor Burhanettin Tugan; U.S.A., Dr. Osborne A. Brines. The vice-presidents for Canada, Mexico, and Czechoslovakia, Dr. J. E. Pritchard, Dr. Luis Gutierrez Villaegas, and Professor H. Sikl, respectively, were unable to be present.

Immediately after the opening ceremony, Sir Lionel Whitby gave his presidential address on "The Science and Art of Medicine." In the evening the Minister of Health received members of the Congress and their ladies at Lancaster House; earlier the council of the British Association of Clinical Pathologists and the executive committee of the Congress had entertained the vice-presidents and the principal speakers to a buffet supper at Apothecaries' Hall.

In all 600 members of the Congress registered, and they came from 37 countries. The mornings and evenings from July 17 to 20 were devoted to scientific papers. In the afternoons visits were arranged to the Lister Institute, the Central Public Health Laboratories at Colindale, the National Institute for Medical Research, the Wellcome Museum, the Wellcome Research Laboratories at Beckenham, Glaxo Laboratories, and the Research Laboratories of Messrs. May and Baker Ltd. Throughout the week a series of scientific demonstrations were on view at the London School of Hygiene and Tropical Medicine, where there was also an exhibition of scientific equipment. On three afternoons films of scientific and general interest were shown.

Official Entertainments

Receptions were given to the members of the Congress by the Vice-Chancellor of London University, the President and Fellows of the Royal College of Physicians, the President and Council of the Royal College of Surgeons, and by the President and Council of the British Medical Association. The British Association of Clinical Pathologists held a soirée at the Goldsmiths' Hall by kind permission of the Prime Warden and Court of the Worshipful Company of Goldsmiths. The Congress terminated on July 20 with a banquet, held at Grosvenor House, at which the speakers included Dr. W. Russell Brain, Dr. S. C. Dyke, Dr. D. Jaumain, of Brussels, Sir Henry Dale, Dr. F. William Sunderman, of Atlanta, Georgia, President of the American Society of Clinical Pathologists, Professor R. Kourilsky, of Paris, and Sir Lionel Whitby.

Scientific Programme

The scientific work of the Congress was divided among four Sections, dealing respectively with microbiology, haematology, chemical pathology, and histopathology. In addition there were two joint sessions on "Pigment Metabolism and Haemoglobin" (Sections of Chemical Pathology and Haematology) and on "Skeletal Disease" (Sections of Histopathology and Chemical Pathology). This week we print an account of the proceedings of the Sections of Microbiology, Haematology, and Chemical Pathology. Next week we shall give a report of the two joint sessions and of the meetings of the Section of Histopathology.

I. SECTION OF MICROBIOLOGY

Non-bacterial Pneumonias

Professor S. P. BEDSON (London) was in the chair at the opening session.

Professor C. H. STUART-HARRIS (Sheffield) opened with an account of diagnostic difficulties in pneumonia. Even with full bacteriological investigation, no pathogenic organism was cultivated from the sputum in a significant number of cases (13% of 109 cases of pneumonia in Sheffield during 1950–1). The majority of such cases were atelectatic or aspiration pneumonias in subjects with chronic bronchitis, but a few resisted chemotherapy, and such included possible cases of virus or rickettsial pneumonia. Cases of primary atypical pneumonia were often diagnosed by the discovery of radiological changes in cases thought to be simple pyrexia, bronchitis, or influenza. Laboratory investigations were needed to establish the causative agent concerned, which might be psittacosis or ornithosis virus, the rickettsia of Q fever, influenza virus, or an unidentified virus agent.

Professor G. LÖFSTRÖM (Upsala) said that cases of atypical pneumonia with significant titres of cold agglutinins were not uncommon in Sweden and had occurred in several small outbreaks. In children such cases might be confused with pulmonary tuberculosis. No virus causative of atypical pneumonia had been recovered in Sweden. Psittacosis was uncommon. Q fever had not been found.

Dr. M. GATMAN (Sheffield) described the results of an investigation of the cold haemagglutination reaction in a variety of cases of respiratory infection. He referred to the need to standardize technique, and instanced factors, such as differing sensitivities of the red cells, effect of concentration of cells, and methods of reading, which influenced the titre. Though a high cold-agglutinin titre had been obtained in two cases of atypical pneumonia and in many of the relatives of such cases investigated in 1950, high titres had also been found in 1951 in pneumococcal pneumonia and influenzal pneumonia. It was difficult to accept that reaction as of value in differentiating atypical pneumonia from other respiratory tract infections.

Dr. B. P. MARMION (London) described investigations with sera sent to the Central Public Health Laboratory from cases of pneumonia or of suspected atypical pneumonia. Complement-fixation tests incriminating influenza and psittacosis viruses and the agent of Q fever were found in a number of instances where the clinical picture suggested an atypical pneumonia. He then went on to describe the identification of *Rickettsia burneti* in England and Wales in cases of respiratory disease. An extensive epidemiological survey with sera from blood donors indicated that Q fever occurred chiefly in Kent and Devon, but scattered infection had been detected widely in the Midlands and the West Country. Areas chiefly affected appeared to be those with large cattle herds. Cattle had been shown to be a source of infection, and there was suggestive evidence of infection in sheep.

In the discussion, Professor A. LINDAU (Lund) referred to false positive Wassermann reactions with sera from cases of atypical pneumonia, Professor S. P. BEDSON mentioned that psittacosis caused a definite percentage of cases of the atypical pneumonia syndrome, and Professor STUART-HARRIS referred to high titres of cold agglutinins in the serum from cases of fulminant influenza virus—staphylococcal pneumonia.

Smallpox

This session was under the chairmanship of Dr. C. G. CULBERTSON (Indiana).

Professor A. W. DOWNIE (Liverpool) said that in eight of the last ten years smallpox had been introduced into the United Kingdom, and these outbreaks had provided opportunities to study the spread of infection and to test laboratory methods of diagnosis. The medical officer who suspected smallpox could obtain laboratory confirmation within 24 hours if suitable material from the focal rash was submitted. Discussing the various diagnostic tests used in 93 cases in Liverpool, the speaker said that the most certain method was to isolate the virus by egg inoculation. In fulminating cases virus was found in 0.1 ml. of blood, and infection might be so heavy that the patient's serum could act as antigen. Failure to isolate virus from throat swabs during the pre-eruptive stage supported the common view that patients were not highly infectious until the rash had appeared. Epidemiologists tended to make deductions on a fixed 12-day incubation period, but there was no doubt that this could be as short as nine days. Unequivocal evidence of infection being transmitted during the pre-eruptive period should be based on a single, and only possible, contact with the infective case at that stage of illness.

Professor M. KAISER (Vienna) described the diagnostic skin test of Tièche, of Zurich, which gave a result within a few hours. Material from a suspected case of smallpox is injected intradermally into an individual, who is kept in a highly allergic state by repeated vaccination. The method can be made free from risk by heating the vesicle fluid in boiling water for five minutes. In tests made with pustule fluid from a child suffering from Kaposi's varicelliform eruption the strain of vaccinia virus proved to be heat-resistant. Lesions in volunteers and in rabbits produced by this heated virus were similar to those caused by living virus. This heat-resistant strain might prove valuable for the preparation of dry vaccine for use in the Tropics.

Dr. W. E. B. HALL (Pennsylvania) described eight cases of foetal smallpox observed during a large outbreak of smallpox in the U.S.A. In a ninth case there had been no apparent contact of the mother with the disease, but she had been vaccinated three weeks before the miscarriage of a 16-week foetus. Immunological observations suggested that the disease was transmitted across the placenta only after completion of the mother's incubation period, and the foetus then developed the disease after its own incubation period. In the foetal skin the lesions were vesicular but not pustular, and in the brain there was a calcareous liquefaction-necrosis with massive destruction of tissue.

Dr. G. BRAS (Java) pointed out that cicatrization in smallpox was mainly confined to the face, and that this was thought to be caused by differences in the structure of the elastic fibres in this area. In necropsy material it had been shown that there was destruction of the well-developed sebaceous glands, and this was followed by organization, retraction, and scarring. Secondary infection played no part in the process. Destruction of the sebaceous glands took place in other areas of the body, but there the glands were scattered and smaller, so that a "moth-eaten" appearance did not develop.

Dr. C. W. DIXON (Leeds) had found that, despite its proverbial infectivity, not all susceptibles were attacked even when exposed to massive smallpox infection. The spectacular cutaneous manifestations had focused attention on the scabs as a source of infection, whereas the spread did not occur continuously but in waves at 13-day intervals. *Variola sine eruptione* and abortive cases argued against the view that the pre-eruptive phase was not infectious. He thought that the virus liberated by the skin might be slightly different from that discharged by the respiratory route.

Dr. F. O. MACCALLUM (London), speaking of the Brighton outbreak, referred to a patient with a single minute lesion on the sacrum from which virus had been recovered; by egg-culture there were 30 virus particles per 0.1 ml. of serum. A needle-scraping of a single pustule in another patient several hours before the generalized rash had given a heavy growth of virus. Two patients, who had been vaccinated eight years previously, had had a fleeting scanty rash, but smallpox was confirmed by serological tests.

Bacterial Typing

Dr. G. S. WILSON was in the chair for this session, which was devoted to the bacteriophage typing of *Staph. pyogenes*.

Dr. R. E. O. WILLIAMS (London) described the technique of identifying strains of staphylococci by their phage reactions. He indicated certain broad groups of phage-types, and pointed out that one such group (6/47) was associated with food-poisoning and also included most of the penicillin-resistant strains isolated in Britain. He emphasized the value of phage-typing in tracing the source of an outbreak of staphylococcal infection. R. WAHL (Paris), after drawing attention to some of the technical difficulties involved, suggested a classification of staphylococci on the basis of phage patterns into four groups, which he related to serological groups. Like Dr. Williams, he found that most penicillinase-producing strains belonged to the 6/47 phage group. Dr. G. WALLMARK (Stockholm) stated that it was at present impossible to draw up a definite scheme of staphylococci on the basis of phage reactions. He described the incidence of various phage-types isolated from patients and staff of many hospitals in Sweden. Finally Dr. MARY BARBER (London) discussed the way in which phage-typing studies had helped to explain the increasing incidence of penicillin-resistant staphylococcal infection in hospital practice.

The serological typing of paracolon bacilli was described by Dr. P. R. EDWARDS (Georgia, U.S.A.), who said that more than 200 antigenic types had been isolated. He gave a classification of these organisms into biochemical and serological groups, but indicated that exact identification was possible only with some strains. The value of attempting to type these bacteria was illustrated, he said, by recent work on gastro-enteritis due to strains of *Bact. coli*. Dr. JOAN TAYLOR (London) described the technique used at Colindale in the identification of salmonella organisms on the basis of the Kauffmann-White scheme of antigens.

A discussion on the serological typing of *Str. pyogenes* was opened by Dr. REBECCA LANCEFIELD (New York). She pointed out that the method of typing was based on the M protein antigen and could be performed by an agglutination or precipitin technique, although different results with the two methods sometimes occurred as a result of another antigen, the T protein. She described some of the technical snags, and discussed the value of typing strains in an epidemic or in the collection of data in rheumatic fever. Dr. G. T. COOK (Oxford) gave examples of types of streptococci isolated in Oxford from both epidemic and sporadic infections, again emphasizing the importance of such studies in elucidating the origin of epidemics.

Laboratory Control of Chemotherapy

This session was under the chairmanship of Sir ALEXANDER FLEMING.

Dr. WESLEY W. SPINK (Minneapolis) began by deploring the indiscriminate use of sulphonamides and antibiotics before a diagnosis had been made. It was a prerequisite for successful treatment that the infecting organism should be identified, and this was sometimes rendered impossible by blind treatment given before admission to hospital. He gave an account of the principal diseases now seen in the medical services of the Minneapolis hospitals: prominent among these were lobar pneumonia, diphtheria (which had sometimes been misdiagnosed), and viral hepatitis. There had been a marked increase in bacteriaemias due to Gram-negative organisms, perhaps originating in the urinary tract. The frequency of penicillin resistance in staphylococci had risen in recent times from 13 to 50%; that organism could also develop resistance to aureomycin, and this change involved resistance to terramycin also. He used a tube dilution method for determining sensitivity: it was highly desirable that a technique for such tests should be generally standardized. A study of the effect of combinations of antibiotics was presented: the use of two drugs together might be the only effective treatment for certain infections, an example cited being combined penicillin and chloramphenicol, which had proved successful, after *in vitro* tests had predicted its efficacy, in overcoming a *Proteus* endocarditis.

Dr. ELEANOR A. BLISS (Baltimore) defined the main tasks of the laboratory in connexion with chemotherapy as verifying the susceptibility of the micro-organism to the chosen drug and determining that the dosage was adequate. Drug assays in blood were usually superfluous with antibiotics but sometimes necessary with sulphonamides owing to variable absorption. Tests of microbic sensitivity to antibiotics must take account of factors affecting drug activity: thus the composition and *p*H of the medium, and in particular its content of serum, etc., the size of the inoculum, and the growth phase of the organism might all affect the result. Some antibiotics also retained full activity after filtration, while others did not. A set of rules was suggested for standardizing conditions in such tests. Many routine sensitivity tests were superfluous: a careful study of all the organisms cultivated in routine examinations during a period at the Johns Hopkins Hospital had shown that the great majority of the organisms had the normal antibiotic sensitivities of their species.

Professor L. P. GARROD (London) maintained that a method of performing sensitivity tests which was to meet the present wholesale demands must be simple: for the benefit of urgent cases it must also be rapid. The cup-plate method in primary culture had these qualities, and gave valuable information. It was sometimes necessary to use more elaborate methods to obtain a more accurate result: he instanced tests of the combined action of pairs of antibiotics which had to be made by means of a series of viable counts in order to show that a combination of penicillin and streptomycin was the most effective against strains of enterococci causing endocarditis. Sulphonamide sensitivity tests, calling for special media, presented greater difficulty than those with antibiotics: two methods for these were described.

Dr. C. GERNEZ-RIEUX and Dr. A. TACQUET (Lille) described two methods for studying the effect of chemotherapy in experimental tuberculosis. One was to follow the antibody titre in the blood by the Middlebrook–Dubos test (agglutination of tuberculin-treated red cells): they had shown that the titre fell during streptomycin treatment in rabbits. Secondly, when inoculation was made intradermally in guinea-pigs the course of the infection could be directly observed and the effects of treatment so assessed. Coloured illustrations were shown of the effect of streptomycin on multiple lesions due to bacilli of which some were drug-resistant: the action of viomycin had been similarly studied.

Dr. R. LINZ (Brussels) discussed the advantages of various methods for testing the sensitivity of tubercle bacilli in sputum to streptomycin. It was desirable that such a test should be rapid, exact, and able to reveal the proportion of resistant organisms to the total. The direct slide method was rapid, but since it used only a small quantity of material it might not give a representative result, bacilli from different areas of lung being known to vary in sensitivity. Test cultures on egg media and in the Tween 80 liquid medium required preliminary isolation, and the latter medium had other disadvantages. The use of a combination of different methods was advocated.

Dr. E. F. THOMSON (Sydney) described a study of the frequency of resistance to four antibiotics of five species of Gram-negative bacilli isolated from numerous patients in the Royal Prince Alfred Hospital, Sydney. The proportion of strains of *Bact. coli* resistant to streptomycin remained constant throughout the period of study at about 50%: the frequency of resistance to aureomycin and other newer antibiotics was rising, but it was hoped that this also might stabilize itself. Other interesting findings with regard to the sensitivities of *Proteus, Ps. pyocyanea*, and other species were reported.

Dr. A. MORABITO and Dr. A. CASTELLI (Rome) had determined the sensitivity to chloramphenicol of strains of *Salm. typhi* from 50 patients by an accurate tube dilution method. The growth of the organism was regularly inhibited by between 2 and 3 μg./ml., and no change in this had been observed in re-isolations during treatment or even after recovery. Professor A. LINDAU (Sweden) commended the cup-plate method for sensitivity tests, inoculating the plate with a standard quantity of a young broth culture made from multiple colonies in the primary plate. Eight cups could be accommodated in one plate, and the medium varied if necessary to suit the species tested, although a standard basic medium of constant composition was desirable. Dr. T. M. VOGELSANG (Norway) advocated the Price direct slide culture method for testing the sensitivity of tubercle bacilli to streptomycin: a result could be obtained in one week. Dr. H. ERICSSON (Sweden) urged that the site and nature of the infection must be considered in adjudging the results of sensitivity tests. Where a high concentration of the drug could be attained, as in the urinary tract, organisms resistant to as much as 100 μg./ml. of an antibiotic such as aureomycin could be successfully attacked.

Infantile Gastro-enteritis

Dr. W. W. SPINK (Minneapolis) was chairman of this session.

Dr. JOAN TAYLOR (London), opening the discussion, described how more work was required on viruses, and more specific methods of identification were needed for some other organisms, before their association with enteritis could be proved. Salmonella epidemics, easy to identify, were of importance in America but uncommon in England. Bray's original observations on *Bact. coli*, which Kauffmann had now placed in his O group 111, had been confirmed in every country where they had been investigated. Tribute was paid to Valne's early work on the serological typing of coliforms. Dr. P. TOLENTINO (Genoa) associated parenteral staphylococcal infection with infantile gastro-enteritis and considered the enteritis was secondary to central nervous lesions. Experimental work on kittens had shown that from infants with gastro-enteritis the nasopharyngeal staphylococci produced enterotoxin 13 times more often than those from healthy infants.

After an infant had introduced *Bact. coli* O group 111 (or O group 55) to nurseries, Dr. Taylor had followed the spread and the association of enteritis with its presence. Dr. G. LAURELL (Tomteboda, Sweden) had investigated epidemics at the Sachs Hospital, Stockholm, in which a similar connexion and spread had been noted. Dr. K. B. ROGERS (Birmingham) described how epidemics had spread through several hospitals, emphasizing that several had been started by infants who were only vomiting. Dr. Laurell thought the transmission of the *Bact. coli* was by nasopharyngeal carriage: he had found "dangerous" nasal carriers whose faeces were clear of these organisms. Dr. Rogers said these infants excreted vast numbers of the *Bact. coli* and showed

how this caused contamination of their environment and articles communal to their ward. Dr. Taylor had failed to isolate these coliforms from over 400 healthy infants, and Dr. Rogers had not isolated them from the necropsy material of 147 infants and children, except from three who had had enteritis and one who had been resident in an infected ward.

Systemic Mycoses

This session was under the chairmanship of Dr. A. CHEDIAK (Havana).

Dr. R. W. RIDDELL (London) stressed the importance of pulmonary lesions in systemic mycoses. In many of these diseases the primary infection occurred in the lung, but, except in actinomycosis, the radiological picture was not sufficiently characteristic to serve as a basis for diagnosis; in fact the resemblance to pulmonary tuberculosis or even neoplasm was often very striking. Dermal sensitivity tests had a very limited use in diagnosis, and the significance of the histoplasmin reaction in healthy persons was still a subject of controversy. The diagnosis of fungus disease therefore depended largely on the microscopical examination of morbid material, and this had been greatly facilitated by the recent introduction of new staining methods, including the periodic acid Schiff technique for the demonstration of fungi in tissues.

Dr. P. HOLM (Copenhagen) enlarged on the synergic theory of actinomycosis, which attributes the disease to the association of *Actinomyces israeli* and certain schizomycetes which may be isolated with it in cultures from the lesions. Neither *A. israeli* nor the other organisms could alone initiate the disease, but after the lesions had been established the destruction of *A. israeli* by the administration of penicillin did not necessarily bring about cure, for the associated micro-organisms, if resistant to the antibiotic, might be able to perpetuate the disease.

Dr. A. NORDEN (Lund) gave an account of his recent extensive studies on the serology of sporotrichosis. The yeast-like form of *Sporotrichum schencki* was used for agglutination tests, autoclaved or ground-up cultures of the fungus as antigen for the complement-fixation test (Kent's technique), and the autoclaved extract for the precipitin tests. With the use of human sera from cases of sporotrichosis, the agglutination test had proved of little diagnostic value, but the results of the other tests indicated that deep-seated or extensive sporotrichosis provoked complement-fixing antibodies and precipitin, but superficial infections might provoke only precipitins.

Dr. R. A. MOORE (St. Louis), describing histoplasmosis, recognized four clinical and anatomical types of the disease: latent or healed focal lesions, active focal lesions without clinical significance, acute and subacute disease, and miliary forms. The diagnosis depends on an adequate mycological examination. The basic pathological changes were parasitism of the macrophages by the fungus *Histoplasma capsulatum* and a type of caseous necrosis. Dr. Moore considered the possibility of the disease being transmitted from man to man through the respiratory tract.

In the subsequent discussion Dr. E. THOMSON (Sydney) referred to torulosis in Australia. Dr. C. CULBERTSON (U.S.A.) spoke of the relative values of serology and dermal sensitivity tests in the diagnosis of mycoses. Dr. J. UNGAR (London) mentioned infection by *Aspergillus niger* from processes where the fungus was used for the production of citric acid. Dr. J. F. MURRAY (Johannesburg) referred to sporotrichosis and histoplasmosis in South Africa.

II. SECTION OF HAEMATOLOGY

Megaloblastic Anaemias

The opening session was under the chairmanship of Sir LIONEL WHITBY (Cambridge) and later Professor P. A. OWREN (Oslo).

Professor L. J. WITTS (Oxford) opened with a discussion on pathogenesis in the light of recent knowledge of vitamin B_{12} and pteroylglutamic acid, its conjugates, and folinic acid. Although vitamin B_{12} and folic acid were chemically distinct, their cellular actions might be interrelated. The use of microbiological assay of serum folic acid was illustrated. The nature of the essential lesion in pernicious anaemia was considered, and particularly the unsettled question whether achlorhydria was the primary factor or simply the result of intestinal changes. Alterations in intestinal bacterial flora might be important. The intrinsic factor of Castle must play a vital part in the absorption of B_{12}, however. Drs. D. L. MOLLIN and G. I. M. ROSS (London) reported the results of microbiological assay of vitamin B_{12} in serum and urine, using *Euglena gracilis* as test organism. The values in untreated pernicious anaemia were far lower than in normal individuals or in non-megaloblastic anaemias. Levels of combined and free vitamin B_{12} in the serum of pernicious-anaemia patients were studied after administration of the vitamin, and falling off in the concentration correlated with bone marrow relapse. Dr. C. C. UNGLEY (Newcastle) described responses in pernicious anaemia to vitamin B_{12} administered by various routes, gauging the results by reference to a standardized, expected dose–response relationship. Massive single doses of up to 3 mg. were effective orally and per rectum, and the responses indicated absorption of up to 1% of the dose. Drs. J. N. M. CHALMERS, W. F. J. CUTHBERTSON, H. F. PEGLER, and Z. M. HALL (London) described the similar haemopoietic activity of vitamins B_{12}, B_{12c}, and B_{12d} in pernicious anaemia. Urine excretion studies of vitamin B_{12} after test administration were carried out by microbiological plate assay with *Bact. coli*. Following intramuscular injection, excretion occurred in health and to a less extent in pernicious anaemia. After oral administration of large doses very little appeared in the urine of either group.

Dr. L. G. LAJTHA (Oxford) summarized his studies on the culture of normal and megaloblastic bone marrow in serum–Ringer media. Megaloblasts developed normoblastically in normal serum, but not in pernicious anaemia serum unless it had been sufficiently diluted, apparently because of the presence of an inhibitor. Normal marrow underwent megaloblastic change in pernicious-anaemia serum. Folic and folinic acids effectively ripened megaloblasts, but crystalline vitamin B_{12} did not do so unless it had been incubated with neutralized normal gastric juice. Dr. G. LARSEN (Oslo) discussed the significance of macrocytosis in pernicious anaemia and liver disease. By mathematical treatment of the Price-Jones curve of dried films the normal cells could be separated from the macrocyte population. The mean cell volume was normal, however, and in wet preparations on non-wetting surfaces the diameter of all cells was normal. The macrocytosis appeared to result from the spreading of the abnormal cells during drying. This was perhaps due to the presence of an abnormal haemoglobin, since the rate of alkali denaturation was slower than normal. In discussion Professor C. RIMINGTON (London) and Dr. H. S. BAAR (Birmingham) stressed the importance of physical studies of abnormal haemoglobins. The final paper of the session was by Dr. A. WILTON (Stockholm), on the tissue biology of pernicious anaemia from the standpoint of mitotic activity and degree of differentiation in megaloblastic marrow and in the haemopoietic tissues of chicks and hens.

Haemolytic Anaemias

This session was under the chairmanship of Dr. JANET VAUGHAN (Oxford).

Dr. J. V. DACIE (London) reviewed modern methods for the study of haemolytic processes and went on to illustrate the use of acidified serum, trypsinized normal red cells, and paroxysmal nocturnal haemoglobinuria red cells in laboratory studies. The value of the Coombs test was stressed, and methods were described for differentiating between reactions due to warm antibodies in haemolytic anaemia and cold antibodies. Dr. S. I. DE VRIES (Amsterdam) dealt with haematological and biochemical changes in infants with minor degrees of haemolytic disease, including red cell and white cell changes and the estimation of serum iron.

Dr. W. H. CROSBY (Boston) described the occurrence of haemoglobinaemia, haemoglobinuria, and haemosiderinuria in haemolytic diseases, and related them to the severity of the haemolytic process. Dr. S. MOESCHLIN (Zurich) and others discussed therapy of haemoglobinuric transfusion reaction, and Dr. Crosby said that alkalis were dangerous. Dr. L. G. MOMIGLIANO (Turin) then read a paper on pathogenesis of congenital haemolytic icterus with spherocytosis, stressing the role of the spleen in producing the latter.

Laboratory Aspects of Blood Transfusion

Dr. OSCAR B. HUNTER, sen. (Washington), was chairman of this session.

Dr. P. L. MOLLISON traced the discovery of the incomplete form of the anti-A iso-antibody, and discussed how this and the anti-A haemolysin might be demonstrated. The presence of these types of antibody was often associated with previous inoculations, particularly of tetanus toxoid and T.A.B. vaccine. Haemolytic disease of the newborn could arise from the development of maternal anti-A iso-antibodies. Dr. MARGARET PICKLES (Oxford) dealt with the standardization of the methods for acting upon red cells with proteolytic enzymes, whereby they became sensitive detectors of incomplete antibodies. With certain systems such as the Kell, the receptor loci on the cells were destroyed by the enzyme treatment. Dr. G. DISCOMBE and Dr. H. MEYER (London) demonstrated the reliability of the rapid capillary tube method of rhesus grouping, statistically analysing their series for internal homogeneity and comparing it with the results of other workers using different methods on comparable populations. Dr. W. D. DOLAN (Arlington, Va.) described his experience in maintaining a blood bank in a small general hospital; the use of disposable recipient sets was a noteworthy point, and avoidable reactions were very rare. Dr. H. C. CHAPLIN (London) described the negative results of a controlled investigation into the use of a phenothiazine compound (R.P. 3300) as a possible means of prolonging the viability of stored blood.

Endocrinology and Haematology

This session was under the chairmanship of Professor L. J. WITTS (Oxford).

Professor L. S. P. DAVIDSON (Edinburgh) reviewed the use of laboratory animals for studying the relationship between endocrine function and blood formation. A number of quite clearly defined abnormal blood pictures arose following the removal of the pituitary, suprarenals, or thyroid. However, in man, study of the blood of patients suffering from endocrine disorders was often disappointing and diagnostically unreliable. The use of A.C.T.H. and cortisone in the treatment of acute leukaemias, acquired haemolytic anaemias, and thrombocytopenic purpura had proved less effective than was hoped, and in discussion numerous speakers corroborated this. The variable response of the blood eosinophils to A.C.T.H., particularly in Addison's disease, was stressed. Dr. D. ROBERTSON-SMITH and Dr. F. G. J. HAYHOE (Cambridge) reported studies on the peripheral blood response to adrenaline, particularly the raised leucocyte count. The factors involved were complex. Drs. S. MOESCHLIN, J. R. PELAEZ, and F. HUGENTOBLER (Zurich) described the plasma cell response to sensitized rabbits injected with typhoid vaccines. Under phase-contrast microscopy plasma cells in the spleen pulp containing cytoplasmic granules were seen to be abundant after five days. The disappearance of these granules coincided with the appearance of antibodies in the blood.

Blood Coagulation and Haemorrhagic Disorders

Dr. D. E. LUENGO ARROYO (Madrid) was in the chair.

Professor P. A. OWREN and Dr. K. AAS (Oslo) described the function of proconvertin in blood clotting. This was required in addition to factor V (pro-accelerin) for the effective conversion of prothrombin to thrombin. Depression of proconvertin might be an important part of dicoumarol action, and it was important to use a combined measurement of this and prothrombin in controlling therapy. This could be done by a test using asbestos-filtered ox plasma. Dr. R. BIGGS and Dr. R. G. MACFARLANE (Oxford) described a case of pseudohaemophilia appearing in adult life in a female. The disease appeared to be due to the presence of an inhibitor in the gamma-globulin which acted by neutralizing the anti-haemophilic globulin. Dr. P. DE NICOLA (Pavia) gave the results of various investigations of the clotting mechanism for the reliable control of anticoagulant therapy. Dr. J. F. ACKROYD (London) described work on the pathogenesis of "sedormid" purpura which suggested that the substance might combine with platelets to produce an antigen. In sensitive individuals an antibody was formed which caused lysis of the agglutinated platelets in the presence of complement. Dr. W. JACOBSON and Dr. R. D. MERCER (Cambridge and Boston, Mass.) described evidence for an increase in circulating heparin-like substances in acute leukaemia which could be titrated by use of protamine. These anticoagulants appeared responsible more for bleeding than for platelet reduction, and daily oral doses of 3 g. of lysine lowered the levels and lessened bleeding.

The Erythrocyte

This session was under the chairmanship of Dr. S. I. DE VRIES (Amsterdam).

Professor M. MAIZELS (London) opened with an account of active cation-transport in human erythrocytes. Contrary to the view that the erythrocyte was a dead and passive cell, it had been shown that it engaged in active cation-transport, and that this process was dependent upon the intracorpuscular glycolytic system. In stored cells some potassium was lost but a greater amount of sodium gained; the addition of glucose reversed these changes. Dr. G. ASTALDI and Dr. P. TOLENTINO (Pavia and Genoa) described marrow culture studies on cases of thalassanaemia. The results suggested an inherent cellular defect with a diminished maturation of the basophilic erythroblasts independent of the external medium. Dr. J. FIELDING (London) showed that erythrocytes agglutinated in acid salt solutions which were isotonic but of low ionic strength. Different *p*H values for maximum agglutination were observed for washed cells and cells in the presence of serum. Cells in serum behaved like globulins around their iso-electric point, and evidence was presented that they adsorbed globulins on their surface.

Disorders of Erythropoiesis

Dr. S. MOESCHLIN (Zurich) was in the chair at this session.

DI. B. VAHLQUIST (Upsala) read a paper on aplastic anaemia in which erythropoiesis was predominantly affected, usually appearing early in life and quite easily controlled by transfusion. Dr. E. NEUMARK (London) spoke on the clinical features and post-mortem findings in various examples of aplastic anaemia. Dr. A. PINEY and Dr. M. S. ROSS (London) presented details of a patient in whom sarcoidosis had been demonstrated by histological section of the aspirated bone marrow. A large spleen infiltrated by sarcoidosis was subsequently removed. Dr. G. ASTALDI, Dr. E. BERNARDELLI, and Dr. E. RONDANELLI (Pavia) described studies on the haemopoietic tissues of young chick-embryos. The determination of the mitotic index was not very informative, but, by comparing this with the progressive increase in the number of cells in arrested mitosis following colchicine injection, a much better evaluation of the rate of proliferation could be made. Dr. GRETA HAMMARSTEN (Stockholm) concluded with a description of macrocytic anaemias experimentally induced in rats, mice, and guinea-pigs by ligation of the common bile duct and splenectomy, and which could be prevented by injection of ox-spleen extract following operation.

III. SECTION OF CHEMICAL PATHOLOGY

The opening session was under the chairmanship of Professor E. J. KING (London) and later Professor G. F. MARRACK (London).

Dr. R. M. ARCHIBALD (New York) gave an inaugural address entitled "Frontiers of Biochemistry." He stressed

the need for the chemical pathologist to be cognizant of developments in all fields of pathology, as workers in other disciplines tended more and more to use biochemical tools to advance their knowledge. As the histologist's interest was applied to smaller units, and as the chemical pathologist studied larger molecules of colloidal systems, their fields of inquiry tended to meet.

Dr. J. B. FOOTE (London) discussed methods of investigating thyroid function with radio-iodine and gave results of a clearance technique based on thigh and neck measurements. Drs. B. L. DELLA VIDA and E. A. RAGGIO (Rome) reported a titration technique for uric acid estimation in plasma, claiming greater accuracy at high concentrations than with colorimetric methods. Professor OMAR KHAIRAT (Egypt) described experiments to produce an accurately graduated proteinometer. Dr. J. A. GRIFOLS (Barcelona) introduced 4-aminoantipyrine into phosphatase estimations, obviating the need to precipitate proteins.

The remainder of the session was devoted to papers on protein fractions. Electrophoretic separation of the fractions in serum by a filter-paper technique was described by Drs. E. KÖIW, G. WALLENIUS, and A. GRÖNWALL (Upsala) and its application to cerebrospinal fluid by G. WALLENIUS (Upsala). The flocculation tests were discussed by Dr. N. H. MARTIN and Professor N. F. MACLAGAN (London) and by Dr. P. DE NICOLA (Pavia). Dr. J. GRAS (Barcelona) described fractional curves of serum protein with sodium hyposulphite.

General Metabolism and Nutrition

This session was under the chairmanship of Dr. A. DURUPT (Paris) and Professor R. A. PETERS (Oxford).

In an introductory paper Professor E. J. BIGWOOD (Brussels) described the application of some of the newer chromatographic methods of analysis to the determination of the composition of food proteins. Dr. C. E. DENT (London), speaking on the medical applications of paper chromatography, described some of the "patterns" of amino-acids normally present in urine and those present in cystinuria, Fanconi's syndrome, and Wilson's disease. From comparisons with plasma patterns it would appear that some renal abnormality, presumably of tubular reabsorptive function, must play a part in the production of these urine patterns. He showed also that arginine and lysine might occur in the urine of cystinurics. Dr. J. O. LAWS (London) dealt with the differing fates and excretory products of radioactive proteins after injection into immune and non-immune rabbits.

Dr. H. M. SINCLAIR (Oxford) emphasized the value of the biochemical analysis of tissues (erythrocytes, leucocytes, or hair) rather than of fluids such as plasma or urine in the study of nutritional diseases. He also stressed the difficulties in interpreting blood analyses in these conditions, and referred to work in his laboratory on the part played by fatty acid and vitamin A deficiencies in the production of follicular hyperkeratosis. Dr. A. ROSSI and Dr. E. DI LEVA (Rome) described the estimation of blood pyruvate by a method involving separation by paper chromatography. Professor R. H. S. THOMPSON (London), speaking on blood pyruvate levels in polyneuritis, emphasized the need for caution in assuming that raised levels necessarily indicated thiamin deficiency. Dr. J. N. CUMINGS (London) described investigations on the urinary excretion of copper and amino-acids in four cases of Wilson's disease treated with dimercaprol. Three of the patients were improved both clinically and biochemically and showed temporary increases in urinary copper excretion during this treatment.

Hormones

This session was under the chairmanship of Professor E. C. DODDS (London) and Dr. P. M. F. BISHOP (London).

Professor B. A. HOUSSAY (Buenos Aires) described the use of the toad *Bufo arenarum hensel* for the bio-assay of pituitary and certain sex hormones. Females could be used for the assay of progesterone, being sensitive to 1–5 μg. Males were 100 times as sensitive as females to chorionic gonadotrophin provided they were kept within a critical temperature range of 20° to 30° C. Dr. J. CHEYMOL (Paris) thought that the toad was unsuitable for quantitative chorionic gonadotrophin assays, being insensitive and subject to seasonal variations in sexual activity. To distinguish between chorionic and pituitary gonadotrophin he recommended assays of the same sample of urine using the rabbit and mouse, the latter being more sensitive to pituitary than to chorionic gonadotrophin. Professor E. J. BIGWOOD (Brussels) described the separation of chorionic gonadotrophin from human urine on Chamberland filters at *p*H 3. Paper-strip electrophoresis revealed two components in the separated material, the one moving faster containing all the activity in the Friedman test. Professor G. F. MARRIAN (Edinburgh) said that chemical methods for the estimation of oestrogens were not accurate, while those for the determination of 21-carbon atom adrenocortical steroids were entirely unsatisfactory. Mlle. O. CREPY (Paris) found that the "phenolsteroid" excretion (which included the oestrogens) was very high in the first few days of life in infants, falling to *nil* by the fifth day. It was also raised in male homosexuals and men with gynaecomastia.

Dr. G. I. M. SWYER (London), Dr. P. K. HAMILTON (Bethesda, Maryland), and Dr. A. QUERIDO (Leyden) also gave communications.

Electrolyte Balance

This session was under the chairmanship of Dr. R. M. ARCHIBALD (New York) and Professor R. A. MCCANCE (Cambridge).

Dr. S. E. BRADLEY and his colleagues from New York discussed the effect of the adrenal medullary hormones, and showed that, while their cardiovascular effects were very different, adrenaline and *nor*adrenaline had the same renal effect—i.e., a diuresis with sodium and potassium retention. This was due to a direct effect on the kidney, and occurred even when there was impaired cortical function, as in Addison's disease, and also in a denervated kidney. It occurred with doses insufficient to alter the systemic blood pressure. Dr. D. A. K. BLACK (Manchester) followed with a careful consideration of the renal mechanisms involved in the regulation of sodium excretion. Dr. F. T. G. PRUNTY (London) discussed the effects of cortisone and A.C.T.H., and showed that, while desoxycorticosterone was ineffective in restoring normal diuresis to a patient with Addison's disease, the further addition of cortisone was able to do this without increasing sodium loss; further, in a patient with dermatomyositis and oedema, cortisone and A.C.T.H. had produced immediate release of oedema fluid. It was apparent from this discussion that the control of water and salt excretion was complicated, and determined by a balance of hormonal actions.

Drs. G. K. MCGOWAN (Bristol) and S. W. STANBURY and M. D. MILNE (Manchester) described electrolyte excretion in nephrocalcinosis. The discussion following their papers tended towards the view that the Lightwood and Albright syndromes and the Fanconi syndrome were all closely related and even possibly varying manifestations of similar abnormalities.

Dr. A. GRÖNWALL (Upsala) described the properties of various dextran solutions as a function of their molecular weight distribution, and showed how it was possible to predict the way the kidney would deal with such a solution if the molecular sizes were known.

Dr. W. W. PAYNE (London) and Dr. A. JORDAN (Sheffield) described rather disappointing results in the use of cation-exchange resins in the treatment of nephrotic oedema and hypertension: good results were obtained at first, but continuation was unsatisfactory and there was danger of hypokalaemia, dehydration, and acidosis.

Dr. E. M. DARMADY and his colleagues from Portsmouth described a method of estimating blood and plasma volumes and extracellular space simultaneously by the use of P^{32} for

the red cells and I^{131} for plasma, with inulin for the extracellular space. Two papers by Dr. F. F. HITA (France) and Dr. J. HARKNESS (Portsmouth) dealt with sedimentation rates. Dr. Harkness pointed out that plasma viscosity had an advantage over sedimentation rates, as it could be determined on older specimens of plasma.

TUBERCULOSIS AND DISEASES OF THE CHEST

A Festival Year Conference on Tuberculosis and Diseases of the Chest, sponsored by six specialist societies, was held in Oxford from July 16 to 21 under the patronage of Lord Moran, who gave the opening address. There was an excellent supporting programme of social events, including a reception by the Mayor, a garden party in St. John's, and a dinner. In addition to the sessions reported below there were papers on "Results of British Mass Radiographic Surveys," by Dr. Norman Smith; "Vaccination with the Vole Bacillus," by Dr. A. Q. Wells and Dr. J. Young; and on "Bronchiectasis in Children," by Mr. A. L. d'Abreu and Dr. J. H. Hutchinson.

M.R.C. Tuberculin Survey

Dr. MARC DANIELS reported the results of a large tuberculin survey organized by the Medical Research Council in 1949–50, for which the actual field work was done by the staff of the local authorities. Individuals aged 5–20 years in 22 selected areas were tested by a standardized technique, using first a P.P.D. jelly on a site prepared with flour-paper, followed if negative by the intradermal injection of 100 tuberculin units of old tuberculin as a final test dose. Tests were completed on over 94,000 children and young adults. The selection of cases at school age was satisfactory, with consent rates of over 80%. The 15–20-year age group was possibly less representative, but the inclusion of a group of National Service men aged 18–20 years helped to produce a balanced picture. The results had been analysed for age groups of the two sexes and for three types of area—rural, south urban, and other urban. All groups showed an increase in the proportion positive with increasing age; the increase was from 10% positive at age 5 years to 60% positive at age 20 years in the south urban group; for the other urban group the figures were higher, rising from 14% to 73%. At age 5 years the rural group showed 20% positive, and the figures remained above those for the urban groups throughout school life, but at age 20 years there were 65% positive in the rural areas, a figure between those for the two urban groups. The high rates in rural children were almost certainly due to milk-borne infection, and there was some confirmation of this in the results for individual areas: in a rural area (Cheshire), where most milk was retailed raw, high tuberculin-positive rates were found in children, while in another rural area (Montgomery), where pasteurized or T.T. milk was available throughout the county, very low tuberculin-positive rates were found in children. The highest of the urban rates occurred in a group of industrial towns closely associated with a rural background, where a good deal of raw milk was drunk.

For each type of area there was little or no difference between the sexes at school ages, but from age 12–14 years up to age 20 years the male rates were higher than the female rates. If annual infection rates were calculated from the percentage positive in successive age groups, an almost constant conversion rate was found during school life, but there was a definite increase in this rate after leaving school.

Treatment of Tuberculous Meningitis

Opening the session on the treatment of tuberculous meningitis Dr. HONOR SMITH showed that with streptomycin alone the survival rate was 60%. Routine studies during the course of treatment had shown certain characteristic changes starting between the fourth and fourteenth days; there was a systemic reaction accompanied by wide fluctuations in the cell count in the cerebrospinal fluid, in which the protein content at first increased, with a later fall. There was reason to believe that this response was due to release of tuberculo-protein from destruction of bacilli. Evidence for this was obtained by the intrathecal injection of P.P.D. into normal subjects; there was invariably a characteristic response in tuberculin-positive individuals, but little or no response in tuberculin-negative individuals. Desensitization of the skin of positive individuals did not abolish the meningeal response, but vaccination of negative individuals with the vole bacillus led to a characteristic response about the time that skin sensitivity developed. To test this reaction still further, intrathecal P.P.D. was given to an almost moribund case of tuberculous meningitis not responding to streptomycin; to everybody's surprise there was clinical improvement, and from this a scheme of treatment for such cases had been developed, using intrathecal P.P.D. and streptomycin. The method had been used in 22 cases and was undoubtedly dangerous, but did give results in some cases otherwise hopeless. It was suggested that the mode of action was by resolution of tuberculous exudate. Dr. Honor Smith finished with a plea for the reassessment of the place of tuberculin in treatment now that streptomycin was available for use with it.

Professor R. S. ILLINGWORTH gave the results of streptomycin treatment of 82 unselected cases of tuberculous meningitis in children. In one-third of the cases the disease was advanced before treatment was started, and he emphasized the importance of early diagnosis if good results were to be obtained. This applied not only to the number of cases surviving but also to the final condition of the survivors. It was among the cases which were advanced when treatment was started that gross physical and mental defects were ultimately seen; serious defect was rare among the survivors of those in whom treatment was started early. Experience had taught that hope of recovery should not be abandoned short of the development of a state of decerebrate rigidity; however, late relapse after apparent recovery was also a real possibility.

Chemotherapy of Tuberculosis

The session devoted to the present position of chemotherapy in tuberculosis was opened by Dr. J. W. CROFTON, who first reviewed the various groups of drugs which had been tried in tuberculosis. Nothing of clinical value had been derived from other bacteria, but there were several antibiotics from fungi. Streptomycin was the most outstandingly successful; its dihydro derivative had been abandoned as too toxic. Viomycin was a promising new preparation, but it was already known that resistance to it did occur. Neomycin was too toxic, but "terramycin" might find a place in association with streptomycin. Of plant derivatives great claims had been made in Japan for cepharanthin, but independent trial in animals by Feldman had shown no activity. Of synthetic drugs the most important was *para*-aminosalicylic acid, especially for its action in checking the development of streptomycin-resistance in a considerable proportion of cases; in this connexion Dr. Crofton was of the opinion that streptomycin and P.A.S. should always be given together, never one without the other. P.A.S.-resistance did occur, and once it had developed P.A.S. no longer protected against the development of streptomycin-resistance. The sulphones might have some action in delaying the development of streptomycin-resistance, but were of little value alone. The thiosemicarbazones undoubtedly had some action alone, probably less than P.A.S., but their effect on streptomycin-resistance was not known. Finally there was a group of drugs elaborated by Barry and his group in Dublin (see also *British Medical Journal*, July 28, p. 233); B.53 was probably too toxic, but B.283 was promising, though possibly its greatest use would be in leprosy. Dr. Crofton then discussed the theoretical background of streptomycin treatment, especially the development of resistance; he

produced good evidence for his view that this was due to mutation rather than adaptation.

The papers by Dr. L. E. HOUGHTON and Dr. C. CLAYSON dealt with the results of chemotherapy and showed a considerable measure of agreement. In particular it was apparent that chemotherapy alone was frequently insufficient to achieve permanent control of the disease. Its great value lay in preparing patients for well-tried collapse measures and as protection during and after major surgical procedures. Thus, Dr. Houghton could claim only 10% good results from chemotherapy alone in cases with gross cavitation, but 69% good results when chemotherapy was followed by collapse therapy in such cases. In Dr. Clayson's series control of the disease was obtained in one-third of the cases by chemotherapy alone; in a further one-third it was necessary to follow this with collapse therapy before control was achieved. Dr. Houghton expressed the view that streptomycin (as distinct from P.A.S.) should be reserved for a critical phase in the patient's illness, and this might mean withholding its use until the patient was in hospital. This view did not receive universal acceptance in discussion, though it was agreed that the first course was the most effective. Dr. Houghton referred also to the administration of P.A.S. by the intravenous route, a method he hoped to try shortly, and to a patient intolerant to both streptomycin and P.A.S. who was now being treated without reactions by the concurrent use of A.C.T.H.

Surgery of Mitral and Pulmonary Stenosis

One afternoon was devoted to four papers on cardiac surgery; the excellence and completeness of these were sufficiently demonstrated by the absence of any discussion or questions. Mr. R. C. BROCK dealt with intracardiac surgery, which he had employed in 160 cases with an overall mortality of 18%. Many of the deaths had occurred during the early period of its use, and the mortality for the later part of the series was little over 5%. Even the diseased heart tolerated these procedures well, but he had abandoned the use of 4% procaine in the pericardium and was now using 5 ml. of 0.25% solution of decicaine.

Mitral valvulotomy was rapidly becoming a standard procedure for the treatment of mitral stenosis, and the operation could no longer be regarded as a desperate measure. He had operated on patients aged 19 years, but under that age there was a considerable danger that active rheumatism might still be present; if so, operation was contraindicated. Practically the only other contraindication was a large heart with aneurysmal dilatation of the left auricle; auricular fibrillation, thrombosis, and embolism were unfavourable features but were not contraindications. The results in survivors were almost uniformly excellent, only three being regarded as poor. The popularity of the operation and the demand for it were a pleasing testimony to the effectiveness of the method.

Turning to congenital heart disease, Mr. Brock pointed out that, while the Blalock type of operation was undoubtedly successful in many cases, there were objections to the production of an artificial ductus arteriosus, and any underlying pulmonary stenosis tended to be progressive. He was therefore turning more and more to direct intracardiac procedures to eliminate pulmonary stenosis, using an approach through the wall of the ventricle. For pure valvular stenosis this was the only reasonable operation, and even for cases of infundibular stenosis and Fallot's tetralogy he was using the method to an increasing extent.

Coarctation of the Aorta

Mr. C. PRICE THOMAS said that coarctation of the aorta was a relatively common abnormality occurring in the adult form in 1 in 1,500 of the population, and in 1 in 750 if the infantile form was included. The diagnosis of the condition rested primarily on the recognition of hypertension in the upper limbs combined with hypotension in the lower limbs. The presence of dilated collaterals reinforced the observation, and the condition could be demonstrated by angiography. The prognosis in untreated cases was serious: 25% of them did not survive 20 years, 50% only reached 40 years of age, and 10% only survived more than 50 years, the patients dying from congestive failure, rupture of the aorta, cerebrovascular accidents, or bacterial endarteritis. The optimum age for operation, from both patient's and surgeon's point of view, was about 7 years; the walls of both the aorta and the intercostal vessels were normal and withstood the strain and stress of the operation more satisfactorily, and the possibility of a Goldblatt mechanism arising was less than in the older age group. The question whether or not asymptomatic cases should be submitted to operation was still *sub judice*, but in this group it was the practice at present not to submit to operation those patients with palpable femoral pulses in whom the hypertension in the upper limbs was not severe. All cases with symptoms should be treated by operation. The results to date were very encouraging.

Patent Ductus Arteriosus

Mr. OSWALD TUBBS reviewed 93 cases of patent ductus arteriosus on which he had operated. The diagnosis depended mainly on the classical machinery murmur, present in all his cases, though he recognized that there were cases in which it was absent. Every case over the age of 7 years should be operated on, and operation should be done earlier if the condition was causing symptoms or cardiac enlargement. He had operated on one patient aged 49 years with symptoms, but in patients over 25 years with neither symptoms nor signs of cardiac strain the need for operation was open to question. He had operated on 80 uninfected cases, with two deaths. Only one of the 78 survivors had a diastolic murmur, indicating that closure had been obtained in the remainder. Infected cases should first be controlled with penicillin, though before it was available surgical closure had cured two-thirds of the infected cases. One of the most striking features in all these cases had been the subjective improvement even in those who had denied symptoms before operation.

Constrictive Pericarditis

Mr. T. HOLMES SELLORS concluded the session with a paper on constrictive pericarditis. Clinically the chief feature of this condition was impedance of diastolic filling. The cause of the condition was almost invariably tuberculosis. Cases were seen at one of three stages. (i) Cases seen with a pericardial effusion should be watched for two to three years until the active process subsided; operation should be performed only later, when the constructive process had developed. (ii) Cases presenting with polyserositis should similarly be watched until the acute stage had passed. Frequently ascites was the presenting feature. (iii) Finally there was an older group presenting with signs of fully developed constriction, frequently with massive calcification of the pericardium. Preparation for operation consisted of rest, restriction of fluids and the use of diuretics, and aspiration of ascites in some cases. All cases should be considered for surgery, though generalized tuberculosis was a contraindication. The object of the operation was to remove the greatly thickened and adherent visceral and parietal layers of the pericardium from the ventricles. Damage to the coronary arteries had to be avoided, and it was not so necessary to strip the venae cavae and auricles. Mr. Holmes Sellors had seen 46 cases and performed pericardiectomy in 33, with six deaths and 20 good results—i.e., ability to resume useful work. The tuberculous aetiology had been proved in 27 of the 33 cases. In some cases in which only small amounts of pericardium could be removed, unexpectedly good results had followed.

Pneumoconiosis of Coal-miners

On Thursday Dr. C. M. FLETCHER opened with a paper on dust inhalation and disability of coal-miners. He distinguished clearly between silicosis and the pneumoconiosis of

coal-miners, in which inhalation of coal dust played a major part. At the M.R.C. Pneumoconiosis Research Unit they recognized four radiological categories of simple pneumoconiosis, progression from one to another occurring only under conditions of exposure to coal dust, but not normally associated with severe disability. The really disabling condition was "progressive massive fibrosis," and this was progressive even in the absence of further dust exposure. There was reason to believe that a factor in addition to dust was responsible for this, probably infection, most probably tuberculous infection, though there were difficulties about accepting this hypothesis. They were putting the hypothesis to practical test in the Rhondda Fach scheme, where, with the aid of the regional hospital board, they hoped to remove all, or most, of the sources of tuberculous infection in one area, in order to see if there was then a fall in the rate of development of progressive massive fibrosis in miners known to have simple dust disease. Much could be done to prevent dust disease by improved methods of dust suppression in the mines, but they believed that the efficiency of such methods should be controlled by periodic examinations of all miners.

Social Aspects of Tuberculosis

Dr. J. E. GEDDES discussed rehabilitation and resettlement. He estimated the magnitude of the problem from a sample of 940 notified cases of pulmonary tuberculosis in Birmingham. The problem was not so great as might be thought, as many had returned to their previous work, and the number unemployed or unsuitably employed was small in this survey—about 10% of arrested and quiescent cases. Comparatively few active cases were at work, but a considerable proportion of those that were working were doing unsuitable work. For a city with a population of one million he calculated that there would be 1,270 cases under treatment, equally divided between the sexes, 390 requiring sheltered employment, but 45 would be over the age of 55 and only 9% of them women; and a further 350, of whom 160 would be over the age of 50, unemployable because of tuberculosis, in the ratio of two men to one woman. Such estimates rapidly became out of date because of the changing epidemiology of tuberculosis; of male cases notified in Birmingham in 1935 and 1940 23% were alive five years later, but of cases notified in 1945 57% were alive after five years. The fall in mortality between 1939 and 1950 had been much greater at young adult ages than in older age groups, especially for males. Dr. Geddes then described a "disability index" devised by Brieger, based on calculated relapse rates, physical stability, physiological fitness, and respiratory function.

In conclusion he suggested that the present organization of the rehabilitation and resettlement services must recognize that the goal of clinical and preventive practice—full physical restitution—might well be within reach.

Pulmonary Resection in Tuberculosis

The final discussion was on pulmonary resection for tuberculosis. All three speakers agreed that resection had a place in the treatment of conditions such as destroyed lung, empyema and broncho-pleural fistula, persistent cavitation under a thoracoplasty, and broncho-stenosis for which there was no other effective treatment. Where collapse therapy, including thoracoplasty down to the seventh rib, was feasible, Dr. F. H. YOUNG preferred it as a routine measure until the long-term results of resection were ascertained. He preferred resection to complete thoracoplasty.

Thoracoplasty was a proved operation, giving in the hands of Mr. VERNON C. THOMPSON and his colleagues sputum conversion in 94% of cases, with a mortality of just over 1%. Mr. RONALD EDWARDS, on the other hand, had extended his indications for resection to include tension cavity, cavity under a pneumothorax, and collapsed segment under a pneumothorax; as an experimental procedure he was including fibro-caseous disease, even if bilateral in some cases. Finally there was a group of round foci, which Dr. Young showed might arise in a number of ways; there was also the difficult differential diagnosis from carcinoma of the bronchus in these cases. The general view was that these foci should be removed if large, possibly by subsegmental resection, but there was some difference on the size which called for removal. All speakers were agreed that resection should not be employed for acute or recent disease, and that most careful assessment based on a long series of *x*-ray films was essential. Mr. Edwards put it that the patient must have got over the acute phase of the disease, whilst Dr. Young preferred to wait until maximum benefit had been obtained from conservative measures. The condition of the contralateral lung was important, and Mr. Edwards required that if disease was present it must have been stable for at least one year. The differences in approach may be judged from the fact that Mr. Edwards reported a series of 420 cases submitted to resection, whilst Dr. Young reported 80 cases submitted by the Brompton physicians to the surgeons in 1949–50, and Mr. Thompson's series consisted of 60 cases. The difference in operative mortality, which was at the low level of 2.4% in Mr. Edwards's series, must also be partly attributable to the more favourable type of case on which he was operating.

SHORTAGE OF CHILD PSYCHIATRISTS IN LONDON

A committee on juvenile delinquency set up by the London Council Council has lately issued its report to the Council.* The committee consisted, in addition to members of the council, of representatives of the Churches, of the London Council of Social Service, and of other organizations. It included one medical member, Dr. Alfred Torrie, representing the National Association of Mental Health.

In its report, which ranges over the whole field of child care, the committee states that a survey of psychiatric services in London indicates a need for additional child-guidance clinics, particularly in the south-western and south-eastern areas of the county. The chairmen of the metropolitan juvenile courts are of opinion that many children find their way to the courts as being beyond control or as offenders because attention to their problems is too long delayed owing to long waiting-lists for child-guidance clinics or through lack of vacancies at suitable residential schools.

The committee regards the early detection and suitable treatment of subnormal, maladjusted, and ineducable children as of the utmost importance. Apart from the shortage of child-guidance clinics there are far too few child psychotherapists; many of the existing clinics are staffed by insufficiently trained personnel; there is not at present any complete or really adequate training in child psychiatry, as the six months allocated under the existing regulations for the Diploma in Psychological Medicine are not enough. The problem is regarded as calling for urgent consideration. It is realized that trained staff are difficult to obtain, but it is hoped that special consideration will be given to the employment of psychiatrists to work in infant-welfare clinics. The wider use of problem-case conferences and the development of the child-guidance service are urged so that diagnosis and treatment can be effected more expeditiously. It would be an advantage if it were made possible for any responsible person who suspects maladjustment in a child to be able to refer the child direct to a clinic or centre for diagnosis and treatment.

Another recommendation of the committee is that adequate arrangements should be made for the after-care of all educationally subnormal children after they have left school, especially those who are not reported by the local education authority as needing supervision under the Mental Deficiency Acts.

*Unpublished.

Correspondence

Medical Practice on the Gold Coast

SIR,—In his letter (July 21, p. 179) "Goldcoaster" complains about the threat to "the high standards of [medical] work and ethics" on the Gold Coast which could result from a decision to widen the registration qualifications there. But does he call it a high standard of work which is being offered when there is only one doctor to 65,000 people (his own figures)? Or does he think it a high standard of ethics to deny medical care to 19 patients out of 20 so that the twentieth can be treated by British standards? He is not to blame for this situation, and is much to be admired for seeking in high personal standards an escape from an impossible social situation, but a clear division must be made here between personal virtue and social policy. The majority of Africans are faced with the choice not between good medicine and poor medicine but between any medicine or none at all, and in a world shortage of doctors society must surely seek to make the best use of whatever medical knowledge and ability are to be found. The quality of European refugee doctors varies very much, as I know from long experience with them, but there were many fine ones among them, and a board including people with some knowledge of the group could easily have selected people who would have been exceedingly valuable in our Colonies. What is to be regretted is not that we are now thinking of recruiting them but that we are so late about it, for most of them have now resettled, often in non-medical work, and we have lost some fine surgeons and specialists to the U.S. Pacific Islands, to Israel, and to America.

Under these circumstances it seems regrettable that a medical man should quote with approval the narrow Civil Servant comment on "dilution," a comment which is appropriate to certain trades and professions where the supply of skilled or trained man-power is ample but which is most inappropriate to Africa. Surely "dilution" of medical knowledge so that it can reach everyone in some degree instead of only a few is exactly what is required, and one might have expected the Colonial Office to have sponsored the employment of only half-trained doctors, such as some countries had to do during the war and as Russia does in her more sparsely covered countryside. Under such circumstances the status of the old Colonial medical officer, with ability, would still be quite assured or even improved, for with an understanding policy he would be used as consultant, and paid as such. Such a policy might even raise medical standards, not reduce them, for much of to day's medical responsibility is inevitably left to the nurses and orderlies, and if these were given the opportunity to raise their status in two or more stages they might become more ethical.—I am, etc.,

London, S.W.20. H. B. M. MURPHY.

Post-coital Tests and Infertility

SIR,—Professor T. N. A. Jeffcoate's article (July 21, p. 167) should be of great help to all those interested in the problem of infertility, whether in general practice or specializing in gynaecology. We do, however, think that his condemnation of the post-coital test is too forthright, as we feel that valuable information may be gained from it by those who have had some experience in the interpretation of the macroscopical and microscopical appearances of the cervical secretions after intercourse at the ovulatory period of the cycle.

Scanty tenaceous mucus poorly invaded by sluggish or inactive sperms often indicates poor oestrogen secretion which will respond to appropriate treatment. Mucus from an apparently normal cervix may, on microscopical examination, be found to be full of desquamated cells, pus, and organisms and scantily invaded by inactive sperms. After treatment with sulphonamides and penicillin the mucus is often found to be clear and well invaded by active sperms. The persistently negative post-coital test may be the only indication of some error in coital technique in a husband and wife who appear perfectly fertile on all other investigations. Post-coital tests with subsequent appropriate medical treatment can be carried out as out-patient procedures, whereas dilatation of the cervix as recommended by Professor Jeffcoate necessitates admission of the patient to hospital for several days. The wives of men whose semen shows a moderate or low fertility sometimes have a surprisingly good post-coital test. The prognosis in these cases is correspondingly improved.

From the experience of large numbers of these examinations we should say that it is unusual for pregnancy not to occur when this test is repeatedly good in the absence of any organic cause for infertility.—We are, etc.,

M. MOORE WHITE.
London, W.C.1. E. MARY POLLOCK.

Torsion of a Pyosalpinx

SIR,—I was greatly interested and a little surprised to read Dr. Joseph Wolf's article (May 12, p. 1062) on what was stated to be a relatively rare condition. In view of this I felt that it might be worth while placing the following case on record.

A nurse of 36 was admitted complaining of continuous knife-like pain in the right loin and right iliac fossa, of eight hours' duration. This then subsided for a few hours, but had been getting worse during the 24 hours prior to admission. There was no nausea, vomiting, or dysuria, and her bowel habit was normal until the onset of this attack, since when she had been constipated. Her periods were regular, and her last ceased with the onset of the attack. There was no vaginal discharge. She had had two previous but less severe attacks in the past two years.

On examination her temperature was 99° F. (37.2° C.), pulse 72, respirations 20; tongue furred; foetor oris noted. There was marked tenderness and rigidity along the whole of the right iliac fossa extending up towards the right loin. Rovsing's sign positive. Marked tenderness all over hypogastrium. Rectal examination was normal, and so were the respiratory and cardio-vascular systems.

A diagnosis of acute (retrocaecal) appendicitis with pelvic peritonitis was made.

At operation an oedematous appendix was found lying over the fimbriated end of a large right gangrenous pyosalpinx, which measured approximately 5 in. by 2 in. (12.5 cm. by 5 cm.) and was twisted three times in an anti-clockwise direction. The right tube and appendix were removed and the wound closed without drainage. Unfortunately no biopsy was made of the pyosalpinx. Culture showed a profuse growth of *Bact. coli*.

—I am, etc.,

Taunton. H. H. W. JACKSON.

Prevention of Coronary Thrombosis

SIR,—Dr. R. Halstead Dixon (July 21, p. 179) refers to the value of correct breathing in the prevention of thrombosis and recommends special breathing exercises in an attempt to reduce the scourge of coronary thrombosis. In the course of examining large numbers of young people aged 15 to 18 I have been concerned to find that the great majority do not know how to breathe, and have little or no understanding of why they breathe. Physically they are, on the whole, good specimens, but few could be described as fit, and most have indifferent posture. Surely an elementary knowledge of physiology and the why and how of respiration and posture should be a basic part of education and physical training in all schools. Simple health education and pride in physical fitness might do much to reduce the incidence of certain diseases, and incidentally help to relieve doctors of unnecessary work.—I am, etc.,

Farnham Royal, Bucks. M. E. M. HERFORD.

Vegetarians and Atherosclerosis

SIR,—It occurred to me, while reading the concluding remarks of Dr. J. B. Firstbrook's slightly alarming but interesting paper on atherosclerosis in its newer aspects (July 21, p. 133), that investigation of strict vegetarians on the lines he suggests should give useful information. It would, I imagine, be fairly easy to find a matching control group of normal eaters for comparison, and vegetarians would surely be co-operative in tests so likely to provide them with medical and scientific support for their dietary code.—I am, etc.,

London, S.E.1. MAY ELLIOT.

Antihistaminics and Burns

SIR,—I read with great interest the letter from Drs. A. E. Milne, K. C. Balfour, and J. P. Yeoman (July 14, p. 117) on the use of antihistaminics in the treatment of burns. It suggested to me that I might report three cases of burns treated by immediate application of local antihistamine cream. Even with minor burns there may be appreciable absence from work, especially if there is blistering of the hands. In all these cases the local reaction was considerably less than might have been expected, and the loss of working time consequently reduced.

Case 1.—A girl canteen worker aged 17. A large jug of boiling water was spilt over the backs of both hands and wrists. She was seen almost immediately and complained of severe pain. A thick covering of "anthisan" cream was applied. The next day there was slight patchy redness on the backs of the fingers but no blistering. She complained of soreness. The dressing was renewed and she returned to work the following day without further treatment.

Case 2.—A painter aged 32. The flame of a blow-lamp being used to take paint off a door was accidentally diverted across his face. He was seen five minutes later. The whole face was covered with a black deposit, and he complained of intense burning sensations. A thick dressing of anthisan cream was applied. Four hours later the face was red and rather tender. The dressing was replaced. The next day there was slight redness only and no blistering, and he returned to work.

Case 3.—A boy mill worker aged 17 exposed his arm to a number of small steam jets set ½ in. (1.3 cm.) apart used for treating cloth. He was seen 15 minutes later. The whole of the flexor surface of the forearm from elbow to wrist was tender and painful. A dressing of anthisan cream was applied. The next day there was some redness of the forearm but no blistering. He returned to work on the fourth day.

These results suggest that antihistamines may be of value as an immediate treatment for minor burns. I have found that application after about four hours has passed seems to have no effect on the development of redness and blistering although pain is partially relieved. It is difficult to be certain what is the maximum time that can elapse before the treatment loses its value without a further trial on a large number of cases.—I am, etc.,

Leeds A. J. LEVINE.

Rh Grouping

SIR,—With regard to Dr. J. Murray's letter (July 14, p. 118), may I give evidence in support of the Chown capillary method? I have been using this method for over three years, after a careful and prolonged comparison with the standard tube technique, which showed absolute agreement. The number of tests since carried out is 2,700, of which 470 were negative with anti-D serum; this gives 17.4% negatives. Over 90% of our tests are on antenatal patients; the negatives are all subsequently tested for antibodies and the rhesus grouping is confirmed by the North London Blood Supply Depot. On only two occasions were false negatives reported, and these were both subsequently shown to be D^u positive. I am convinced that with a careful technique this method is reliable.—I am, etc.,

London, W.C.2. SIDNEY SHAW.

Films in Medical Teaching

SIR,—I regret that my remarks at the Conference on Methods in Medical Teaching have given the impression to Mr. Michael Essex-Lopresti (July 14, p. 116), and perhaps to others, that I am not in favour of the use of films. This has probably occurred because I chose to devote this talk mainly to the effective use of lantern slides, while merely touching on other visual methods such as films. I did this purposely because the lantern slide is seldom given serious consideration. I agree with Mr. Essex-Lopresti that there are few suitable films available for teaching. The large number of medical films made yearly are sponsored mainly by two groups, commercial firms and individual doctors, neither of whom have as their prime object the teaching of medicine. Films made by commercial firms usually suffer from the disadvantage of being a form of publicity—i.e., they must appeal to a variety of audiences. Medical men film operations, procedures, or treatments which they have devised, and, although the results may be useful as records or, occasionally, as a form of advertisement for the individual or hospital, they are of little help to the student.

If successful teaching films are to be made, they will have to be sponsored by medical men who are directly concerned with teaching, and they will cost more. An appreciation of the medical outlook is necessary on the part of the film technician, and more important still is a knowledge and understanding of the film medium by the sponsor. He must have a clear idea of the information to be conveyed and of the type of audience aimed at. If clinical material is worth filming it is also worth the cost of copying. If this has been done the record will be available to producers of teaching films who wish to exploit the ability of a film to juxtapose material. Because the costs are heavy the results must be good enough to be lasting and to be made use of by all teachers of the subject dealt with. It is only when universities and teaching institutes take the trouble to organize not only film distribution but production facilities that suitable medical teaching films will become available.—I am, etc.,

Paddington, W.2. PETER N. CARDEW.

"War" and "Peace"

SIR,—A questionary is being circulated to doctors by the Central Medical War Committee asking for details likely to be useful in a "fresh state of emergency," which is a euphemism for atomic war. I would suggest that there should be very serious consideration on the highest intellectual and moral planes of the relationship of this request to the Hippocratic Oath. We are taught to endeavour always to preserve life, yet we are now being asked to assist in a policy devoted to its mass destruction. Doctors are the servants of society, but this does not carry any obligation to assist that society in its own destruction. Rather should they hinder such an act.

The causes of the present state of tension are many and complex, and it is not certain how many are under our control. But it is quite certain that the present unfolding of events is proceeding much faster than we ourselves would like, and recent news shows how difficult it is to disentangle ourselves from a given warlike policy once it is started. In a very short time considerations of "face" will make any show of second thoughts impossible. The destruction of all that we are kidding ourselves we are trying to preserve will then probably be inevitable. It is this probability which should be the supreme consideration, and not the details of political hysteria.

I suggest, Sir, that the Hippocratic principles and the existence of the Central Medical War Committee and its recent circular are incompatible at the present time. When a state of war exists there is a good case for the existence of this war body, but when alternatives to war still exist, as is the case, then there are good grounds for calling it the Central Medical Peace Committee, which would devote its work accordingly. I hasten to add that I am not a Communist

and have no particular inspiration from Moscow, but am appalled at being invited to assist in a one-direction programme for the destruction of human life on a vast scale. If war is prevented millions of lives will be spared; if I attempt to save lives in an atomic air raid I will probably save one or two if I am very lucky. One way, several million people live; the other, millions die and nothing is gained. I can see no logical ground for justifying medical help for the present policy at the present time. Better ways of saving life than expending valuable time and money in medical support of atomic warfare are available.—I am, etc.,

Liverpool. H. E. VICKERS.

"Lysivane" in the Treatment of Parkinsonism

SIR,—In an unselected group of 150 patients attending a large general hospital for the treatment of parkinsonism I have used the synthetic drugs "diparcol," "artane," "parpanit," and "lysivane," and it has been possible to compare their clinical efficacy. Attempts to classify the possible aetiology of the disease in the treated patients have not been very successful, but the cases were considered to be principally of the degenerative type, only four post-encephalitics being seen. At the beginning of the trial of the new drugs diparcol, artane, and parpanit were interchanged in the same or comparable patients. The results of using these three compounds showed that clinically diparcol was the most toxic, artane was effective but less so than lysivane, and that parpanit was the least effective. These three drugs were all more effective than solanaceous alkaloids with which many of the patients had been previously treated. The assessment of the results was based on any improvement in the patients' ability to perform everyday acts, upon effects on their morale, and on clinical observation by other doctors beside myself. All claims to improvement were checked so far as possible from evidence voluntarily given by relatives and friends. It is impossible to record progress by measurement of tremors, because they are too easily influenced by emotion and environment.

During the past 18 months I have treated with lysivane 52 cases of parkinsonism, also mainly of the degenerative type. Except in a few instances the superiority of this drug over all others previously used has been such that I am now adopting it as the routine treatment. It has been given in a dosage of 0.05 g. every six hours at the start, and gradually increased to 0.05 g. every two hours during the day, the dose being temporarily reduced should troublesome side-effects develop.

Of the recent series treated 20 have had lysivane for 1 year to 18 months, 34 for 6 to 12 months, and the remainder for not less than six months. In no case has there been a relapse if there has been initial improvement, whereas it is my experience, and that of others, that patients responding initially to other new drugs have relapsed later. Of the 52 patients 28 have greatly improved, 12 moderately improved, two slightly improved, nine failed completely to respond to the drug, and one was made worse. This last patient failed to respond to any form of treatment. These favourable results are similar to those reported by Dr. Harold Palmer and Dr. D. J. A. Gallagher (*British Medical Journal*, 1950, **2**, 558), who report a satisfactory response in 11 cases out of 16 (68.7%). In my series treated with lysivane, 77% showed a favourable response. My results may differ in the number of complete failures. Twelve patients in my series of 52 failed to respond significantly (23%), whereas Palmer and Gallagher had only one failure in 16 cases (6.25%). Owing to the small number of cases treated by these observers this may not be statistically significant. J. Sigwald (*Presse Médicale*, 1949, **57**, 819) reported that lysivane was superior to all other forms of treatment in 46 out of 106 cases (43.4%), identical in 29 (27%), and inferior in four (3.7%).

In 20 cases annoying but not serious side-effects of the drug have been observed. There has been drowsiness during the first few days of taking the drug, but this has always passed off and treatment continued uninterruptedly. Nausea, vomiting, and depression have been met with occasionally at the end of the first week of treatment, but after appropriate adjustment of the dosage these symptoms pass off. Dryness of the mouth can be encountered at any time in the treatment and occurred in 15 cases, but did not cause any serious distress.

From the analysis of the evidence forthcoming from this particular trial, lysivane seems to be the drug of choice for initial use in the treatment of parkinsonism. This investigation will be published in detail after a further follow-up period.—I am, etc.,

Birmingham. R. O. GILLHESPY.

Psychiatry in General Practice

SIR,—I feel Dr. H. Crichton-Miller's reference (July 21, p. 175) to my views may be quite unintentionally misleading. I do not "work to a time limit of three weeks," though I often wish I could. I reported a small highly selected group of cases (*Lancet*, June 23, p. 1331), largely suffering from over-tiredness, who responded quickly to simple in-patient treatment. I also expressed the view that there is an optimum length of stay (about six weeks) after which hospitalization may act detrimentally, and that treatment could often be speeded up with advantage.

Dr. Crichton-Miller adds that this time limit (of three weeks) is probably the best that can be done under the N.H.S. But my criticism would be the other way round—that where patients do not have to pay, and where hospital life is made very congenial, certain classes of patient, especially psychopaths, tend to stay far too long.

As regards Dr. Crichton-Miller's final remark that "the official demand for a rapid turn-over of cases conflicts hopelessly with freedom and efficiency in all psychotherapeutic work," I feel I must take up the cudgels on behalf of the N.H.S. It has certainly not been my experience in the three Metropolitan regions in which I work. Like many others I have had my moments of irritation at official communications, but I have never received any directives or even requests concerning the numbers of patients I should see or the time I should spend with them. The limiting factor is not due to any official demands, but the prevalence of psychiatric disorder. And, as I said in my article, it is the commendable self-restraint of the long-suffering general practitioner in referring patients that prevents what facilities there are from being swamped.—I am, etc.,

London, W.1. W. LINDESAY NEUSTATTER.

Preventive Psychiatry

SIR,—Sir Allen Daley (June 9, p. 1279) wrote, "Increasing attention is being given to preventive psychiatry, but, beyond a realization that many cases of juvenile maladjustment and adult mental illness arise from wrong handling of the infant and young child, little is yet known, and even that which is known is seldom applied." I would disagree only with the "little is yet known," for I consider that sufficient is known for us to make a considerable reduction in the incidence of the emotional problems of children and their growth into the mental disorders of adults.

To bring about a change, certain criteria must first be fulfilled: sympathetic attitude, knowledge and understanding, the will to treat. The greatest potential for activity in this sphere rests with the local authorities, and much can be done by encouraging and facilitating the attendance of their personnel at conferences and courses such as those run by the National Association of Mental Health, and by the organization of group discussions, led by suitable invited persons. There need be no further development of the existing service to implement effectively these ideas. Mothercraft classes are only too uncommon, and where they are to be found it is unique for the mother to be prepared in any way for handling the day-to-day emotional needs of her child. A common example is that of toilet training and the disturbing effect of the child who has broken down from

over-zealous training. At the infant welfare clinic a few minutes devoted to a discussion with the mother is an investment that yields big dividends. I have found that ten minutes with a group of six to eight mothers is easy to organize and does not interfere with the efficient running of the clinic. (They should never take the form of talks but always of discussion.) Similar methods can be used in the toddlers' clinic, but with increasing age and increasing complexity of the problem it may be necessary to see mothers by special appointment. Medicine has advanced by doctors doing what they could in answer to the needs of the time and, in the process of so doing, acquiring greater skill, experience, and judgment. The sad plight of the juvenile delinquent and the recidivist, the burden that these are to the community, the harmful focus of influence that they become to others, make it incumbent upon us to do all we can to prevent this unnecessary blight.—I am, etc.,

London, E.2. DAVID MORRIS.

Leucotomy in Persistent Anxiety

SIR,—Dr. G. D. F. Steele is to be congratulated on his account of the patient suffering from persistent acute anxiety (July 14, p. 84). However, I consider that there are certain points which require comment.

(1) What do we know of the causes of the onset of anxiety at that time?

(2) What was the "energetic psychological treatment" applied?

(3) Once organic causes had been excluded, was sufficient effort made to elucidate the aetiology of the anxiety and its persistence?

(4) Why were further electrocardiograms taken in the midst of treatment requiring confirmation from the physician that the symptoms were psychologically determined? It is significant that the patient's condition deteriorated after this and a suicidal attempt was actually made. Was the patient aware of the psychiatrist's doubt of his own diagnosis which required further electrocardiograms? Did this contribute to her deterioration?

(5) Was any real psycho-analytic treatment attempted?

The dramatic improvement following leucotomy was of course due to the release from the stress of the anxiety. We stop the patient from worrying by chopping off the "worrying mechanism," just as the guillotine used to cure the headache. The patient is certainly now able to lead a routine undistressed life, and, short of any other method of improving the patient, leucotomy is from this point of view useful. However, I cannot really believe that a leucotomized patient makes a satisfactory living companion, except to those who are emotionally and intellectually dull. This patient had had apparently a good pre-morbid personality despite the poor family history. Her intelligence and work-record had been satisfactory. Her illness was clearly psychological in nature. Her cure was by psychological castration.

Would not psychological analysis—i.e., psycho-analysis—have done better?—I am, etc.,

London, W.13. AARON LASK.

Corneo-scleral Suture

SIR,—The suture described by Mr. H. B. Stallard (July 14, p. 88) is obviously effective, but its use admittedly requires the services of a skilled assistant, which are not always available. In the Ophthalmological Society's *Transactions* (1933, **53**, 86) I described a simple conjunctival suture which I have used as a routine measure for a number of years, which requires a minimum of assistance, and which I have found to be most valuable in preventing post-operative complications after extracapsular extraction—I do not practise the intracapsular method. The only modification of my original description which has been introduced is to include episcleral tissue, as well as conjunctiva, in the upper suture.—I am, etc.,

London, W.1. R. AFFLECK GREEVES.

SIR,—Mr. H. B. Stallard draws attention (July 14, p. 88) to a corneo-scleral stitch which employs a new method of a stop-knot. This is the Gomez-Lindner-McLean stitch (Leonardi, E., *Chirurgia dell' Apparato Oculare*, 1948, **1**, p. 345, fig. 245). After this stitch had been demonstrated to Mr. B. W. Rycroft in Rome by Professor Leonardi in 1949 it was subsequently introduced to the Royal Eye Hospital and practised by a succession of registrars and house-surgeons. My personal experience of the stitch extends to over 100 cases during the last two years, and I am able to endorse the value which Mr. Stallard places on the stitch and also to agree that a skilled assistant is essential for its use. In this consecutive series of cases, which were mainly intracapsular extractions, no vitreous was lost, although there were several presentations. Timely traction on the suture closed the incision firmly and prevented vitreous escape.

We prefer to tie the stop-knot before pre-placing the suture, and we have abandoned the conjunctival flap as being unnecessary. A limbal section is now made which is firmly held in antero-posterior apposition by this suture: fine-tooth forceps of the Sobhey Bey or Castroviejo type are satisfactory for holding the grooves of the incision. Two tiny peripheral iridotomies are employed, and we have long been convinced of the value of a little air insufflated into the anterior chamber. It is our opinion that this type of stitch with a stop-knot represents an advantage in the surgery of cataract extraction.—I am, etc.,

East Grinstead. GILES ROMANES.

Smell of Coal Gas

SIR,—There was reported recently another serious accident with coal gas, in which three children lost their lives. It is the law that all gas used for domestic purposes must have an ingredient which gives the gas an odour which renders it easy to detect by smell. However, it is clear that this is quite ineffectual as a warning when the victim is asleep. Further, the odoriferous ingredient appears to be not so unpleasant as to prevent domestic gas being commonly used as a means of suicide.

While organic chemists are able to synthesize such a variety of gases for war purposes, I think they ought to be able to make one to be used as an ingredient in fuel gas which would render it irritant enough to awaken a sleeper. It might possibly rule out gassing as a means of suicide, too.—I am, etc.,

Rhayader, Radnorshire. J. D. O'M. POOLE.

POINTS FROM LETTERS

Aspirin and Haematemesis

Dr. ERIC FRANKEL (Wanstead, E.11) writes: During the last five months I have seen six patients under the age of 30 who were sent to hospital after a severe haematemesis, two requiring blood transfusions. None of these people had any previous history of dyspeptic symptoms, and the haematemesis apparently occurred spontaneously in the absence of evidence of other physical disease or mental disturbance. Every one of these patients, however, admitted to having swallowed one or more whole aspirin tablets from ½–3 hours before they began to feel faint, developed nausea, and started to have a haematemesis. The aspirins were taken for muscular pain, headache, and dysmenorrhoea. The patients made a rapid recovery on an ordinary gastric regime and had no further dyspeptic symptoms. Barium-meal examination two weeks after the haematemesis proved quite negative. . . . The occurrence of gastric bleeding after the swallowing of aspirin must be a rare event, as aspirin is probably the most widely used analgesic drug which can be obtained by the general public without a medical prescription, and self-medication is the rule. However, a few unfortunate susceptible people may suffer serious consequences if they swallow the tablet whole on an empty stomach, and I should like to suggest that the manufacturers should label aspirin bottles and containers, "Crush before swallowing."

Waste of Paper

Dr. J. V. L. GRANT (Tamworth) writes: I wonder if a brief letter in the *Journal* would help to limit the flood of blotting-paper that reaches all doctors daily year after year from manufacturing chemists advertising their wares. . . . As I am only one name in the *Medical Directory* I calculate that 20,000 blotters are presumably being distributed on every occasion.

Obituary

J. H. DRYSDALE, M.D., F.R.C.P.

Dr. J. H. Drysdale, consulting physician to St. Bartholomew's Hospital, died in Buenos Aires on July 13, aged 88.

John Hannah Drysdale was born in Buenos Aires in 1862, the son of John Drysdale, who with his brother had emigrated there from Scotland, and of Hannah Dunn of that city. He came to this country at the age of 9 and was educated at University College School and St. John's College, Cambridge. He then entered St. Bartholomew's Hospital, with which he was to be connected for so many years. Qualifying in 1888, he graduated M.B., B.Ch. in 1890. He was house-physician to Dr. James Andrew at the same time as his great friend the late Dr. Herbert Morley Fletcher was house-physician to Sir William Church. After holding this post he returned to the Argentine and qualified there. Not finding the work congenial, he returned to this country and became demonstrator of bacteriology at University College, Liverpool. Thence he returned to work in the pathology department at St. Bartholomew's, first under Dr. Kanthack and then under Sir Frederick Andrewes. The training which he gained there was evidenced by his whole attitude to medicine. He took the M.R.C.P. in 1893 and was elected F.R.C.P. in 1901. At St. Bartholomew's he became casualty physician in 1895, medical registrar and demonstrator of morbid anatomy in 1902, assistant physician in 1904, physician in 1919, and consulting physician on his resignation in 1924—some three years before his retirement was necessary. He was also physician to the Royal Hospital for Diseases of the Chest for many years. After his retirement he lived in a hotel in Buenos Aires but spent the winter at Monte Carlo and the spring in London. Since 1939 he had not returned to this country, but he never lost his close interest in the hospital he had served so well.

Dr. George Graham writes: Drysdale was a very able and much beloved physician. He had ample private means and took so little interest in private practice that he never had a telephone but used to go round to Dr. Morley Fletcher's house if he was compelled to use one. He devoted his time to St. Bartholomew's, visiting the hospital every day and spending some time in the pathology department, in which he took a keen interest. Perhaps his constant attendance partly explained his extraordinary influence on all the people he taught in hospital; he was readily accessible to all who wished to consult him about problems in medicine or about the future prospects of the applicant. He would say that he never gave advice, but would then proceed to discuss all the pros and cons of any proposition, making it quite clear what his advice would have been if he had given it. His knowledge of medicine was very wide, and he used to read carefully each new edition of Osler's *Principles and Practice of Medicine*. He was especially interested in diseases of the heart and lungs and also of the blood. He never accepted the then current opinion that pernicious anaemia was caused by the presence of haemolytic bacteria in the gut, but thought of it as a disease of the bone marrow.

He was an excellent teacher, and always tried to educate his students and make them think for themselves. A very common Drysdale opening gambit was, "Now tell what you know about so and so." To this the safest reply (only possible to an old house-physician) was, "Nothing, Sir." This would lead to an explanation of what he wanted information about and made it easy to discuss the matter fully. He was very popular with students, and the whole hospital was full of the latest "Dropsy" stories. His peculiar nickname was given while he was still a student after he had returned from a holiday and gained some weight, and it stuck to him all his life. In spite of his conspicuous ability and leisure to use it, he wrote very little and was not well known outside the hospital. He was a strong supporter of the proposal to establish university chairs in medicine and surgery, and greatly aided the first two holders of the chair of medicine by his sage advice. He also took a prominent share in the formation of the Paget Club, which was open to members of the teaching staff, and was its first president.

C. M. WEST, *M.C.*, D.Sc., M.B.

Dr. C. M. West, professor of anatomy, University College, Cardiff, died suddenly on July 23 at the age of 58.

Cecil McLaren West, the son of the late Arthur Birt West, was born in Chorlton-cum-Hardy, Lancashire, and educated at Blundell's School and Trinity College, Dublin. While still an undergraduate he acted as C.O. of the medical unit of the Officers Training Corps, an office to which he brought an unbounded enthusiasm and burning patriotism. In 1915 he graduated M.B., B.Ch. and at once became a captain in the R.A.M.C., seeing service on the Western Front (where he won the *M.C.*), Italy, and the Middle East. After demobilization he had a year's hospital work and then returned to Trinity College, Dublin, as chief demonstrator of anatomy. From 1922–7 he was university anatomist. During this time he spent six months at the Carnegie Laboratory of Embryology in Baltimore under the late Dr. G. L. Streeter, for whom he had the highest regard and affection. During these years he held office in the section of anatomy and physiology of the Royal Academy of Medicine in Ireland, first as secretary and later as president, an indication of the high esteem in which he was held by his Dublin colleagues. In 1926 he was awarded the D.Sc. of the University of Dublin for his published research, and a year later he moved to the chair of anatomy in University College, Cardiff, which he graced with such distinction for almost a quarter of a century.

His chief research interests centred in embryology, to which subject he contributed many original papers. It was the very earliest stages of human development which fascinated him most: in 1941 he published an account of a very early human embryo which, as the Dible–West embryo, now occupies an important place in human embryology. For the past six years he had been editor of the *Journal of Anatomy*, a task to which he gave himself unsparingly. No detail was too small for his personal attention, his thoroughness being born of a real love of the English language and a determination that the journal's high reputation for balanced statement and scientific accuracy should be upheld. It always amazed his colleagues that he still found time in those busy years for original investigation, and indeed at this moment papers from his pen are in the press. Apart from his research papers he contributed chapters

to a number of textbooks, including *Cunningham's Textbook of Anatomy* and Jellett and Madill's *Manual of Midwifery*. For many years he had been a member of the council of the Anatomical Society.

E. W. W. writes: By the passing of Professor C. M. West the students of University College, Cardiff, have lost a very dear friend and the Anatomical Society of Great Britain and Ireland a loyal and devoted servant. As a teacher he was wonderfully successful, whether in the formal atmosphere of the lecture theatre or in the more intimate surroundings of the dissecting room. Although he naturally regarded anatomy as a necessary groundwork for future medical studies, to him a university was much more than a place of vocational training: and from him his students took away far more than a mere knowledge of anatomy. Each year he gave a course of lectures on physical anthropology, combining with them, in pre-war years at any rate, visits to zoological gardens in London and Bristol and to such places of archaeological interest as lay within reasonable distance. These lectures were gems and a source of the greatest enjoyment to both sides. As an external examiner in anatomy he was known to students throughout the universities of Great Britain, for his services were in great demand, and at one time or another he had examined at Aberdeen, Bristol, London, Manchester, and Oxford.

During his 24 years in Cardiff Professor West built up from modest beginnings a modern, well-equipped, and productive department. Unfailingly throughout this long time those that worked with him received warm friendship, heartening encouragement, and much sound advice. Himself he drove hard, but for others he was full of consideration, for he was the kindest of men, simple in the best sense of the word, and honest as the day. To the thousands of students who sat under him he was "The Prof." No other title was needed, nor, among a large professoriate, was there any ambiguity. To hear the cheer which greeted "The Prof" when he rose to speak at a students' function (often when he was not down to speak, for they insisted just the same) left no doubt about the place he occupied in their hearts. What he had to say on those occasions was well worth hearing, for he was a gay and happy man with a great sense of fun. It seems strange that we shall not see him again cycling to the College, whatever the weather, or working in his beautiful garden where he spent his leisure hours. But so it is, and in our sorrow we remember his wife, son, and daughters, to whom we extend our heartfelt sympathy.

Dr. GEORGE WALTER MEARNS, who was in the Government Medical Service of British Guiana for twenty-five years, died in London on June 29, aged 55. He was born at Demerara, British Guiana, and educated at Robert Gordon's Technical College, Aberdeen, and Aberdeen University, where he graduated M.B., Ch.B. in 1925. Before entering the university Mearns saw active service during the first world war with the Royal Engineers (Signals). In 1926, after taking a course at the London School of Hygiene and Tropical Medicine, he was appointed Government medical officer at the public hospital, Georgetown, and the next year he became acting resident surgeon, public hospital, Mabaruma, Government medical officer of the North-west District, and port health officer at Morawhanna. In 1928 he was appointed Government medical officer in the Mazaruni district, and in successive years was made senior medical officer to the mental hospital and senior surgeon at the public hospital, Georgetown. After working for a time as surgeon at the Victoria Hospital, Castries, St. Lucia, he returned to Georgetown as resident surgeon and surgeon specialist to the public hospital. From 1938 to 1940 he was the Government medical officer, Canje Highbury District (including New Amsterdam), and he also served for three years as a member of the New Amsterdam town council. Until recently he was Government medical officer of the East Bank District. Dr. Mearns took a keen interest in the activities of the local branch of the British Medical Association and served as a member of the Branch Council. In 1932 he represented his branch at the Annual Meeting in London.

Dr. S. C. Bettencourt-Gomes writes from Georgetown: Throughout his life Mearns retained the dour manner traditionally associated with the "granite city," but beneath a gruff exterior there was a kind and generous nature known only to his close friends, and they were many. His was no changeable friendship—a friend once made was a friend for life. He was an individualist and was often content to plough a lone furrow if that seemed the correct course to him. His tenacity of purpose was such that, having determined to achieve some object, all obstacles had to be overcome at no matter what cost of time and trouble. As a colleague in hospital he was the best of company, a faithful friend, and a very co-operative member of the staff. He will be sadly missed.

Dr. FREDERICK AUGUSTUS L'ESTRANGE BURGES, who was a well-known general practitioner in Birmingham for many years, died in Handsworth on July 8, aged 81. Born in Birmingham in 1870, Burges was the son of the Reverend R. B. Burges, and was educated at King Edward's High School. He studied medicine at Queen's College (the precursor of Birmingham University), and qualified in 1896. After holding a resident hospital appointment he started practice in Hockley, where he remained all his life. A police surgeon for many years and a Post Office medical officer for 50 years, he also built up a large general practice. He was keenly interested in medical politics, being a member of the Birmingham panel committee during the whole of its existence. For many years he represented the panel doctors on the Birmingham insurance committee, of which he was elected chairman in 1929. For his work as honorary secretary of the local medical war committee in the first world war he was awarded the M.B.E. In 1947 he was appointed O.B.E. for his services to the Post Office. Besides serving as a representative at two Annual Meetings of the B.M.A., Burges was chairman of the Birmingham Central Division in 1922. His athletic ability was remarkable, for as a tennis player he was Warwickshire champion for many years and captain of the Warwickshire team that won the All-England county championship in 1909. A keen and devout churchman all his life, he was largely instrumental in preserving the church schools in Birmingham. His religion was so very real to him that he faced death with that equanimity born of true Christianity. A great personality has gone from Birmingham, a city of great medical personalities.—A. B.

Medical Notes in Parliament

Health of Schoolchildren

The House of Commons on July 24 debated the estimates for the Ministry of Education and for the universities and colleges in Great Britain. Opening the discussion, Miss FLORENCE HORSBRUGH said that the dental treatment of children was something of which all should be ashamed, and the blame should fall on the Government. Last year only 717 dentists were looking after schoolchildren's teeth. If there was to be one dentist to every 3,000 children, 1,900 dentists would be needed in England and Wales. The number of children whose teeth were inspected during 1950

had not been disclosed, but in 1949 2,807,000 had been inspected and 1,422,000 had been treated. She feared that the number treated during 1950 would not prove to be large. The Labour Government had known in 1945 that it would be impossible to have a comprehensive dental service for the people of the country without injuring the dental service for the children, and the Government had made its choice. It ought to keep dental skill available above all for children and in that way ensure that a generation with good teeth was growing up. Suggestions had been made that persons not fully qualified should help to look after the teeth of children, but it would be a great setback to the welfare of the next generation. Miss Horsbrugh also asked if medical inspections of schoolchildren were being carried out to the full extent and whether there was a sufficient number of school nurses.

In the course of his reply to the debate Mr. GEORGE TOMLINSON said that it was perfectly true that when the National Health Service was introduced it had interfered with the school dental service. When there were not sufficient dentists to cover the whole country, then the dentists, being human, went to the best jobs. The country had lost something like 250 school dentists, and he thanked the other 717 for having remained with the children. There was now an agreement under which better salaries were paid, and he hoped the Ministry would be able to build up the school dental service again. The rest of the school medical services had gone on almost unimpaired.

The discussion concluded.

Sickness in Government Establishments

Mr. C. OSBORNE asked on July 24 why specialists were appointed from the Medical Research Council to visit Royal Ordnance factories to examine causes of sickness.

Mr. DOUGLAS JAY answered that investigators from the Medical Research Council were asked to examine the working of the Sick Pay Scheme in Government Industrial Establishments because preliminary reports suggested that sick absence had increased since the scheme came in. But no central records of absence had been kept, and until the investigation was finished he would have no reliable statistics on which to take any decision modifying the scheme.

Pneumoconiosis Bill

The Pneumoconiosis and Byssinosis Benefit Bill, 1951, was presented to Parliament by Dr. EDITH SUMMERSKILL, Minister of National Insurance, and given a first reading on July 25. It enables the Minister of National Insurance to provide a scheme under which payments would be made out of the Industrial Injuries Fund to certain persons totally disabled from pneumoconiosis (including silicosis and asbestosis), or from byssinosis, and to the dependants of persons dying from the disease. The proposals cover only persons who have not been insured against the disease under the Industrial Injuries Scheme and who are not entitled to workmen's compensation or civil damages for it.

Beds in Teaching Hospitals

Dr. CHARLES HILL on July 26 asked the Minister of Health what upper limit he had placed on the number of beds which a teaching hospital should contain, and upon what grounds his decision was based. Mr. A. BLENKINSOP replied that in Mr. Marquand's view it was undesirable for acute general hospitals to have more than 700–800 beds.

Cancer Education

Dr. CHARLES HILL on July 26 asked what steps the Minister of Health was taking to organize, or to encourage local authorities to organize, public education on the subject of cancer, to secure the earliest possible treatment for this disease.

Mr. A. BLENKINSOP answered that the Central Health Services Council recently advised that it was undesirable at the present time for any cancer publicity to be carried out by any central Government organization direct to the general public. The Central Council for Health Education is planning a pilot experiment in public education in cancer through local authorities, with which he intended to keep in touch.

Remuneration of Practitioners

Sir HUGH LUCAS-TOOTH on July 26 asked the Minister of Health if he could make a statement regarding the negotiations with the medical profession on the remuneration of general practitioners.

Mr. A. BLENKINSOP replied that the General Medical Services Committee had requested that the matter be referred to arbitration. That request was under consideration.

Aged Chronic Sick

Mr. A. BLENKINSOP stated on July 26 that in addition to about 46,000 chronic sick in hospitals in England and Wales on January 1 there were 22,113 aged or infirm men and 20,306 women in accommodation provided under Part III of the National Assistance Act. All local authorities had been required to estimate the long-term residential provision needed for old people and their proposals for meeting this need in the schemes provided under Section 21 of the National Assistance Act.

Smallpox.—In England and Wales two death certificates were received in 1950 on which vaccination, vaccinia, post-vaccinal encephalitis, or any other complication of vaccination was mentioned, the ages at death being 18 and 67.

Bifocals.—Since the beginning of the supplementary ophthalmic services, bifocals have been provided only as an alternative to two necessary separate pairs of glasses.

Chemists.—The amount outstanding on the claims by chemists for dispensing services at the end of June, 1951, was of the order of £4,250,000. Mr. Marquand is considering whether a further supplementary payment can be made.

Prison Food.—A new punitive diet for prisoners in England and Wales is being devised by the medical advisers of the Home Secretary.

Medico-Legal

MISTAKE IN LOCAL ANALGESIC

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Damages amounting to £2,604 were recently awarded[1] by Mr. Justice Slade against the Greenwich and Deptford Hospital Management Committee and a doctor in an action brought by the widow of a patient. Her case was that her husband died as a result of being given the wrong local analgesic during an operation for removal of a cyst in the neck.

The patient, a barge trimmer aged 32, was admitted to the Miller Hospital in July, 1949, for the operation, which was a slight one and was to be performed under local analgesia. By an unfortunate mistake, instead of the analgesic prescribed pure adrenaline was injected, and the patient died within a few minutes. Liability was admitted by the defendants, and counsel on their behalf emphasized that the last thing they wished was for the widow to be given any figure other than what was fair and reasonable.

In assessing the damages, Mr. Justice Slade said that as the widow was only 33 there was a prospect that she would re-marry, but he must have regard to the fact that her husband was at the time of his death a healthy man aged 32 with a long expectation of life. He left three children aged 11, 5, and 2.

[1] *The Times*, May 8.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending July 14 (No. 28).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

Disease	1951 Week Ending July 14					1950 Corresponding Week					1942-50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	35	2	5	1	1	50	2	12	3	3	680	277	50
Deaths	—	—	—	—	—	—	—	—	—	—			
Dysentery	292	59	82	5	1	222	19	87	1	—	222	156	50
Deaths		—		—			—		—				
Encephalitis, acute	12	—	—	—		8	1	—	—	—	8	2	—
Deaths		—			—		—			—			
Erysipelas			12	1	2			11	3	4			
Food-poisoning	199	21		2		397	16		—				
Infective enteritis or diarrhoea under 2 years				8	34					27			
Deaths	5		—	1	—	9		4	—	2			
Measles*	7,662	187	176	144	162	9,295	647	267	128	321	9,459	5,376	2,536
Deaths		—	—	—	—		—	1	—	—			
Meningococcal infection	33	2	15	2	2	33	1	18	1	—	84	46	17
Deaths		1	—				—	1					
Ophthalmia neonatorum	38	4	8	—		29	1	6	—	—	106	65	29
Pneumonia, influenzal	348	17	2	9	1	315	18	2	1	—	519	387	315
Deaths (from influenza)†	6	1	1	—	—	—	—	—	—	1			
Pneumonia, primary			116					96					
Deaths	129	19		7	3	109	8		7	6			
Poliomyelitis, acute:													
Paralytic	50	1	} 21	} 2	} —	} 212	} 8	} 49	} 12	} 5	} 212	} 19	} 9
Non-paralytic	70	3											
Deaths§	—	—			—	7	—			—			
Puerperal fever			5				—	1		2			
Puerperal pyrexia‖	92	14	3	3	—	67	7	10	4	—	155	123	67
Scarlet fever	802	87	89	14	34	1,175	63	92	47	76	2,095	1,303	845
Deaths		—	—	—	—			—	—	—			
Smallpox	—	—	—	—		—	—	—	—				
Deaths				—					—				
(1) Tuberculosis, respiratory			180	27				176	34				
(2) Tuberculosis, non-respiratory			37	6				19	6				
(1) Deaths	} 126	{ 15	17	2	11	} 137	{ 11	20	2	9			
(2) Deaths		{ 3	1	3	4		{ 4	5	1	1			
Typhoid fever	4	—	1	—	1	3	1	3	—	1			
Deaths¶	1	—	—	—		—	—	—	—				
Paratyphoid fever	29	3	—	1	1	9	2	—	—	1 (B)	56	19	11
Whooping-cough	3,277	193	265	37	104	4,117	256	240	25	62	4,117	2,184	1,098
Deaths	3	1	1	1	2	6	2	—	—	1			
Deaths (0–1 year)	198	21	21	4	12	209	29	31	13	19	340	286	209
Deaths (excluding stillbirths)	4,027	679	452	100	136	4,098	595	514	83	155	4,228	4,002	3,562
Annual death rate (per 1,000 persons living)			9·3					10·3					
Live births	7,214	1,188	857	208	333	7,317	1,219	866	193	348	9,327	7,393	5,894
Annual rate per 1,000 persons living			17·6					17·4					
Stillbirths	184	22	15			153	21	25			233	205	153
Rate per 1,000 total births (including stillborn)			17					28					

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Vital Statistics

Infectious Diseases

The only large variations in the trends of infectious diseases in England and Wales during the week ended July 14 were falls in the number of notifications of measles 882, whooping-cough 81, and dysentery 76.

The largest declines in the incidence of measles were Durham 181, Yorkshire West Riding 169, Devonshire 161, and Lancashire 158, while the chief exceptions to a declining incidence were rises in Kent 176 and Carmarthenshire 102. Only small variations were recorded in the number of notifications of scarlet fever; the largest were a fall of 32 in Lancashire and a rise of 20 in Surrey. The largest declines in the local incidence of whooping-cough were Lancashire 40 and Essex 36; the largest rise was Warwickshire 55. The number of notifications of diphtheria were 13 more than the record low level of the preceding week. The largest variations in the local returns of diphtheria were in Yorkshire West Riding and Staffordshire, where 6 and 4 cases were notified and none in the preceding week.

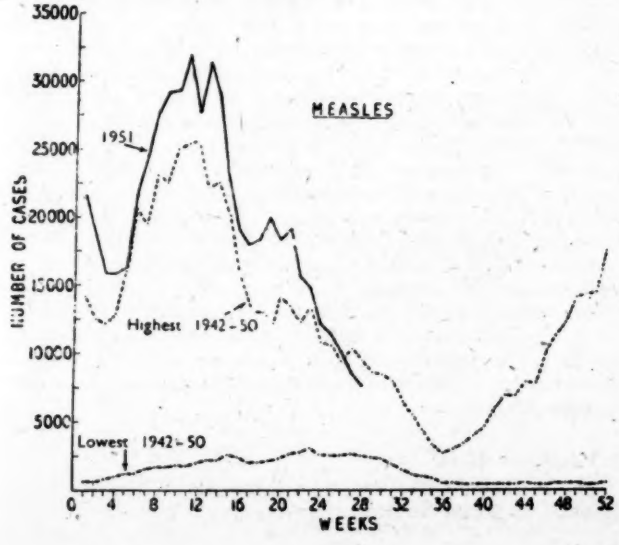
The notifications of acute poliomyelitis were 20 more than in the previous week. There were three distinct centres of infection: Warwickshire, where the cases rose from 16 to 28 (Birmingham C.B. 15, Coventry C.B. 6); Yorkshire West Riding, with a rise from 8 to 21 (York C.B. 7, Sheffield C.B. 5); Kent, with an increase from 4 to 17 (Orpington U.D. 13). The next largest return of acute poliomyelitis was Middlesex 5. A rise in acute poliomyelitis was recorded in Scotland, where 21 cases were notified. Twelve of these cases were notified in the western area (Glasgow 5). The largest return outside this area was 4 in Aberdeen county.

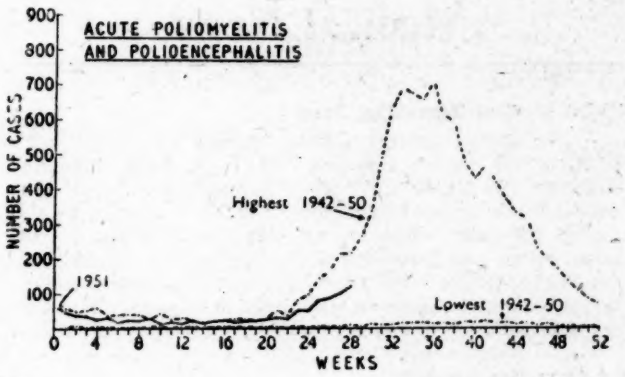
For the third consecutive week a fall has been recorded in the number of notifications of dysentery. The largest returns during the week were London 59 (Islington 13, Finsbury 11), Lancashire 55 (Liverpool C.B. 11, Manchester C.B. 10), Middlesex 26, Yorkshire West Riding 21.

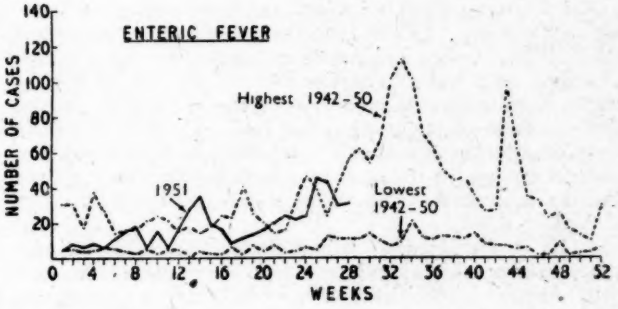
The largest outbreak of food-poisoning involved 72 persons in Tynemouth C.B., Northumberland.

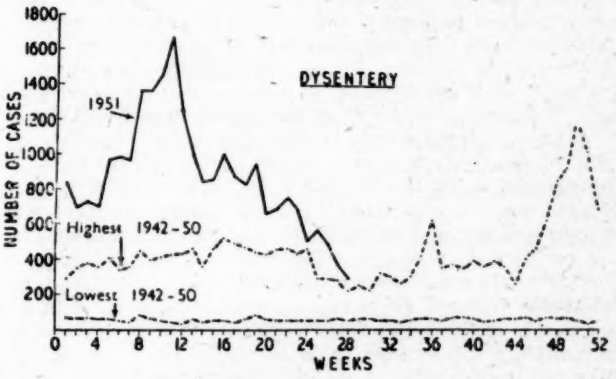
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus -------, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending July 21

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 830, whooping-cough 3,380, diphtheria 30, measles 6,306, acute pneumonia 292, acute poliomyelitis 134, dysentery 301, paratyphoid fever 37, typhoid fever 5.

The number of unsuitable admissions to the Cassel Hospital for Functional Nervous Disorders has been considerably reduced since August, 1948, by the introduction of a new selective procedure (*Medical Director's Report, 1948–50*). Every application used to be made by means of a written clinical description of the patient, sent direct to the medical director, and the decision whether or not to place on the waiting-list was made on this evidence. Now, however, every applicant is interviewed at the hospital, those living a long way away being accommodated for five days, and those from near by being given a day's assessment. Each patient is seen by a psychologist, a psychiatrist, and a psychiatric social worker, who then discuss the case and decide whether or not the Cassel can help the patient. Those selected for treatment are placed on a doctor's waiting-list and sent home to await admission; the others are referred back to their doctor with a full report and other recommendations.

Medical News

Royal Medical Benevolent Fund

At the annual general meeting on July 23 Lord Webb-Johnson was elected president, Mr. F. A. Juler honorary treasurer, and Dr. R. Cove-Smith honorary secretary. The annual report showed that nearly £36,500 was spent in aid during the year, while income was largely made up of subscriptions and donations amounting to over £24,000 and £31,750 in legacies. The Fund maintains a residential home, Westmoreland Lodge, and also beds in a private nursing-home, in addition to giving many forms of individual aid.

"Life in Her Hands"

The first showing of a Crown Film Unit production dealing with nursing, "Life in Her Hands," was given in London on July 27. Among the invited audience were the Minister of Labour and National Service and the Minister of Health, nurses from the provincial hospital where the film was made, and members of the professional cast. The film, which is sponsored by the C.O.I. and lasts about an hour, is for the general public; its object is to stimulate recruitment to the nursing profession. The technical adviser was Sister Ann Ramsden, R.R.C.

"Life in Her Hands" will probably succeed in its purpose. The story is simple: a young widow who holds herself to blame for the death of her husband in a car accident goes into nursing as an escape; we watch her progress from training school to hospital, through the various departments, moving steadily from self-abasement to self-realization, until at the end we see her, happy and confident, playing her part at a desperate "caesar" on one of her friends. The details of hospital life are sympathetically drawn, and there is plenty of humour; the sisters and matron (perhaps a trifle young) are such as one has met, and so are the nurses; the patients could not be bettered. Just occasionally the heroine seems a little slow in a crisis, but by and large the picture is a fair and an inviting one. The technical details are on the whole excellent—especially at the caesarean—though surely noisy shoes clacking down the corridors, and whisky in the ward kitchen (and given by a patient at that), are hardly in the Nightingale tradition. One wonders, too, how often surgeons ask the junior "pro" for a cup of tea in the theatre without a word to the theatre sister. This film can safely be recommended as good instructional entertainment for almost any age.

History and Geography

The recent launching of two new magazines shows that some publishers refuse to be daunted by the crazy costs of producing a journal these days. *History Today* (monthly at 2s. 6d. with illustrations) is a gallant attempt to meet the present popular interest in this subject. Sir Henry Bashford has written entertainingly in it on the history of anaesthesia and antisepsis. *GO* (3s. 6d.), which is published in association with the *Sunday Times*, is a beautifully produced magazine on travel and leisure which rouses in the reader a nostalgia for the foreign scene and the good things of life. Included in the August–September issue is a useful 43-page booklet as a guide to the French Riviera and Provence.

Record Blood Gifts

Donors on the panels of the National Blood Transfusion Service set up two new post-war records in the March quarter this year. There were 141,239 gifts of blood to hospitals in England and Wales, and the number of donors increased to 436,566. New donors recruited during the March quarter number 25,172, but to ensure meeting the steadily expanding use of blood transfusion without calling on the individual donor more often than twice a year, and to provide a reasonable reserve of blood plasma, another 200,000 donors are needed.

Historic Papers in B.M.A. Library

The following papers by L. K. Glinski and English translations, which were referred to by Dr. J. D. Robertson in his article on Glinski and the aetiology of Simmonds's disease in the *Journal* of April 28, 1951, have been presented to the Library: "On some pathological changes of the pituitary gland," *Przeglad Lekarski*, 1913, **4**, 13, "The pituitary gland and its relationship to pregnancy," *Nowiny Lekarskie*, 1913, **25**, 225, 284, 342, 455, "About the hypophysis in general and the changes occurring in this gland during pregnancy." *Klinisch-therapeutische Wochenschrift*, 1913, **20**, 709, 742, 769.

British Association of Urological Surgeons

The seventh annual meeting of the association was held in Glasgow and Edinburgh from June 28 to July 1 under the presidency of Mr. W. W. Galbraith. The report of the council showed that the membership was now 336, and drew attention to the increasing recognition of urology as a specialty. St. Peter's Medals were presented to Mr. R. Ogier Ward and Mr. T. J. Millin. The following were elected officers for 1951–2: President, Mr. E. W. Riches; Vice-president, Mr. T. J. Millin; Hon. Secretary, Mr. A. W. Badenoch; Hon. Treasurer, Mr. R. H. O. B. Robinson; Hon. Editorial Secretary, Mr. David Band. The scientific discussions will be reported in full in the *British Journal of Urology*.

Guidance on Children's Homes

The Home Office has published a memorandum on the conduct of children's homes for the guidance of local authorities and voluntary organizations. It deals with the needs of children who cannot be boarded out and are brought up in children's homes; advice is given on a variety of topics. An atmosphere as much like that in a normal home as possible must be provided. Each child should live as the member of a small group, and the age range should be wide, with boys and girls growing up together. Individual taste should be respected, and there should, for instance, be no uniformity of dress. Recommendations are made about medical arrangements, and a medical officer should be appointed for each local authority and voluntary home. The memorandum is intended to be read with the *Administration of Children's Homes Regulations*, 1951.

Hospital for Kingston and Malden

The South-west Metropolitan Regional Hospital Board last November decided to close down the Kingston Victoria Hospital, which was built by local public contribution as a jubilee memorial to Queen Victoria. The staff of the hospital and the majority of people in the Kingston and Malden area resisted this move, but finally without avail. Believing that the people of Kingston and Malden need the hospital service which the Victoria formerly provided them with, the general practitioners who used to serve on its staff have launched an appeal for funds to convert a large house in the district into a hospital where they can treat their patients. The financial arrangements for treatment in the proposed hospital will be the same as those which prevail in the N.H.S. The funds will go to form a charity called the Kingston and Malden Victoria Medical Foundation. The sum of £50,000 is needed to acquire and adapt the house in question and to maintain it as a hospital for two years. Contributions should be sent to the honorary treasurer, Dr. L. D. de Launay, c/o Barclays Bank, Ltd., Kingston Hill, Surrey. The sponsors of this movement will, it is understood, make a statement to the medical profession in the autumn of this year.

Publications Received

The Welfare of Old People in Rural Areas, The National Council of Social Service.

COMING EVENTS

European Society of Haematology

The Society, under the presidency of Dr. Paul Chevallier, will hold its third congress in Rome, October 3 to 6, at the invitation of the Italian Haematological Society. The programme of topics and speakers will include: Isotopes (John Lawrence, California, U.S.A.), Histochemistry and Modern Microscopy (W. Laves, Germany; H. Lüdin, Switzerland; B. Thorell, Sweden), Reticuloses (Ahlström, Sweden; Van der Meer, Holland; K. Rohr, Switzerland), A.C.T.H. and Cortisone (J. H. Burchenal, U.S.A.), and Coagulation (Jorpes, Sweden; T. Astrup, Denmark). Requests for accommodation and other information should be sent to Dr. H. Torrioli, 24, Via Genoa, Rome, Italy, or to the secretary-general, Dr. Sven Moeschlin, Medical University Clinic, Zurich, Switzerland.

Pituitary and Adrenal Cortex

A symposium on the influence of the hypophysis and the adrenal cortex on biological reactions, organized by the Swiss Academy of Medical Sciences, will take place in Zurich from September 30 to October 3 immediately after the International Congress of Allergists. Information may be obtained from the president of the Swiss Academy of Medical Sciences, Professor G. Miescher, 43, Zurichbergstrasse, Zurich, 44.

Mass Radiology Congress

The first international congress will be held in Sondalo (Sondrio) at the Sanatorium-Village, September 1 to 3. The four main sections of the congress will cover social problems of mass *x*-ray examination, tuberculous chest diseases, non-tuberculous chest diseases, and technical problems. The fee will be 3,000 Italian lire, and full details may be obtained from the Secretariat, Italian Federation for the Control of Tuberculosis, 200, Via Nazionale, Rome.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Edinburgh University (Anatomy Lecture Theatre), August 7, 4.30 p.m., "*Principles in the Pathology of Arterial Disease*," by Professor J. B. Duguid.

Thursday

HORSE SHOE CLUB.—At Medical Society of London, 11, Chandos Street, Cavendish Square, London, W.C., August 9, 5.30 p.m., annual general meeting. Non-members welcome.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Daly.—On July 10, 1951, to Yvette, wife of Anthony Daly, M.D., M.R.C.P., of Little Newcombes, Newton St. Cyres, Devon, a son.

Laycock.—On July 22, 1951, at Pinner, to Lina (formerly Burges), wife of Dr. J. D. Laycock, a son.

MARRIAGES

Gray—Muir.—On July 6, 1951, at St. George's Parish Church, Edinburgh, Oliver Peter Gray, M.B., Ch.B., to Marion Findlay Muir, M.B., Ch.B.

Palmer—Thould.—On June 23, 1951, at St. Peter's, Parkstone, Dorset, David L. Palmer, M.B., B.S., to Patricia J. Thould.

White—Cottam.—On June 23, 1951, at St. Mary Magdalene's Church, Whiston, Rotherham, Yorkshire, Henry Maxwell White, M.B., Ch.B., to Frances Mary Cottam, M.B., Ch.B.

DEATHS

Bishop.—On July 21, 1951, at Hob House, Trebetherick, Cornwall, Mary Frances Bishop, L.R.C.P.&S.Ed., aged 87.

Stewart.—On July 12, 1951, at Colehill, Dorset, Thomas William Stewart, L.R.C.P.&S.Ed., L.R.F.P.S., Lieutenant-Colonel, I.M.S., retired.

Townend.—On July 15, 1951, at his home, 48, Browning Avenue, Boscombe, Bournemouth, Roy Duncan Morrow Townend, M.R.C.S., L.R.C.P.

Weekes.—On July 17, 1951, at Ottery St. Mary Hospital, Devon, Henry Holman Weekes, O.B.E., M.D.

Wright.—On July 17, 1951, at Canford Cliffs, Bournemouth, Frederick Cecil Wright, M.R.C.S., L.R.C.P., D.A., Surgeon Captain, R.N., retired, aged 64.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Rh Incompatibility and Mental Defect

Q.—*Is it true that children who have been successfully treated for haemolytic disease of the newborn, due to Rh incompatibility, are more likely than other children to suffer from feeble-mindedness?*

A.—The most obvious brain damage that may follow haemolytic disease of the newborn is that known as "kernicterus." Infants who develop the syndrome of kernicterus and survive usually show not only signs of motor damage but also mental defect. However, of all infants with haemolytic disease of the newborn (if one includes all those born with a positive direct Coombs test) not more than about 5% of the survivors show these signs. Of course, if only those infants who develop moderate or deep jaundice are considered, the incidence of kernicterus is higher.

There is some evidence that infants who do not display the syndrome of kernicterus may nevertheless have very slight cerebral damage, as judged by the intelligence quotient. This evidence comes from the studies of Gerver and Day (*J. Pediat.*, 1950, **36**, 342), who tested a group of apparently normal infants, all of whom had suffered from haemolytic disease of the newborn with jaundice. They found that the intelligence quotient of these infants was about 10% lower than that of their elder siblings. Such a small difference can hardly be described as mental defect.

In summary, then, apart from the rather small risk that an infant with haemolytic disease of the newborn will survive with signs of kernicterus, he is not more likely than any other child to suffer from feeble-mindedness.

Stellate Ganglion Block for Strokes

Q.—*I would like to know if injection of the stellate ganglion with procaine or any other substance is practised in this country for the relief of paralysis following cerebral thrombosis or cerebral haemorrhage. If these injections are carried out, what degree of success follows and what is the rationale for this treatment?*

A.—The treatment of cerebrovascular accidents by stellate ganglion block was introduced by Leriche and Fontaine in 1936 (*Rev. Chir., Paris*, 1936, **74**, 755), and since then it has been used sporadically in this country. It has never, however, gained as much popularity as in the United States or on the Continent.

When thrombosis or embolism occurs in a cerebral artery, there is evidence to suggest that vasospasm plays an important role in the production of local anoxia of the brain and thus of the clinical picture. Relief of this spasm would therefore be expected at least to lessen the adverse effects upon the brain. In addition, it has been suggested that, if the increased intracranial pressure due to cerebral oedema could be reduced by improving venous drainage, this would also favourably influence the outcome.

The cerebral blood vessels are supplied by sympathetic and parasympathetic nerves, the former by way of the stellate and cervical ganglia to the plexus on the internal carotid artery. It has been shown that these fibres exercise some control over the blood vessels within the brain, and if their impulses can be interrupted vasodilatation results. The most convenient method of effecting this is by infiltrating the stellate ganglion on the side of the lesion with 2% procaine solution. Thus the spasm associated with thrombosis and embolism can be relieved and venous drainage increased, and

one would expect an amelioration of the clinical state. In the case of cerebral haemorrhage, however, where irreversible destruction of brain tissue has taken place, improvement cannot be expected.

These predictions are borne out by the few reports in the literature, which range from enthusiastic recommendation to definite disapproval. The latter came from Mackey and Scott (*British Medical Journal*, 1938, **2**, 1), who, however, had only 10 cases, five of them being cerebral haemorrhages. Recent accounts are more encouraging, and de Takáts (*Postgrad. Med.*, 1949, **5**, 184) reports 50 patients treated with good responses in 41, and Amyes and Perry (*J. Amer. med. Ass.*, 1950, **142**, 15) produced improvement in 28 out of 44 cases. The following factors are important in influencing the results: (1) Cerebral embolism and thrombosis must be carefully differentiated from cerebral haemorrhage, and the diagnostic criteria of Aring and Merritt (*Arch. intern. Med.*, 1935, **56**, 435) are recommended. (2) Stellate block must be carried out as early as possible—but not before it has been determined that rapid and spontaneous recovery is not taking place. In the report of Amyes and Perry 9 out of 10 cases treated within six hours showed improvement. (3) Repeated block is usually needed, and can be carried out every 8 to 12 hours until no further improvement occurs. (4) One would expect the results to be better in the younger patient where irreversible changes such as arteriosclerosis in the blood vessels are not present.

Although the immediate benefit to the patients may be considerable, it is not clear from these reports what the eventual outcome may be, and there is no adequate series of cases yet to help us. However, these latter authors and others who have experience of stellate ganglion block are strongly in favour of its use, for, after all, there is no other active treatment available at the moment for acute cerebral embolism or thrombosis.

Treatment of Skeletal Tuberculosis

Q.—*A young man, aged 20, has a tuberculous ankle-joint, proved by guinea-pig inoculation of material from a discharging sinus. X-ray examination shows no bone focus, only generalized osteoporosis. The chest is clear. Is streptomycin and/or P.A.S. indicated, and, if so, in what dosage?*

A.—This inquiry raises the wider question of the role of streptomycin in the treatment of skeletal tuberculosis in general. Opinion on this matter has not yet crystallized, and clinical research is still going on. It must always be recognized that skeletal tuberculosis is but a local manifestation of a generalized disease, and that the first necessity of treatment is general rest under the best possible conditions—preferably in an open-air country hospital. Streptomycin has not eliminated this requirement. Nevertheless, in the treatment of a fresh lesion most surgeons would recommend, in addition to general treatment and rest for the affected joint, the administration of streptomycin and P.A.S. in a course of treatment extending usually over about three months, provided no toxic reactions occur. A common dosage is streptomycin 0.5 g. twice daily by intramuscular injection and P.A.S. 5 g. three times a day by mouth. The benefits to be expected from this treatment are still the subject of investigation. It is possible that in children, if adequate treatment is begun early enough—that is, before there is any erosion of articular cartilage—a painless movable joint that will last a lifetime may be obtained; but such a result is unlikely in adults. In both children and adults, if there is destruction of cartilage of bone of the articular surface, it is still unwise to aim at a permanently movable natural joint. Even though recrudescence of the disease might be prevented, secondary degenerative changes necessitating further treatment would have to be expected. As in the past, it still seems better if articular damage is evident to resort to arthrodesis when the disease has become quiescent, or in exceptional circumstances (such as bilateral hip disease) to undertake arthroplasty later.

Effect of Meals on Myasthenia Gravis

Q.—*A patient of mine, aged 34, is the subject of myasthenia gravis. Before the disease was diagnosed she was unable to walk a hundred yards without great effort, and in going up stairs she had to have assistance. She now takes one tablet of "prostigmin" every three hours and carries out her household duties with ease. Provided she goes without breakfast she can go to the market or walk long distances without fatigue, but if she is tempted to eat before she sets out, or to have any food while out, she becomes very weak and has difficulty in reaching home. I have tested this extraordinary phenomenon on many occasions and the result is always the same: she can tackle anything so long as she does it on an empty stomach. Can you give any explanation of this?*

A.—The most probable explanation of the facts in this case is that the patient is having far too little prostigmin for her moderately severe myasthenia. The 15-mg. tablet, when its absorption is delayed by the taking of food, is proving ineffective in relieving her symptoms, especially when they are aggravated by exertion. Also, it is probable that the patient is not taking prostigmin during the night.

Although it is not possible to prescribe for a patient that one has not seen, a dose probably four times that at present being given would appear to be necessary, along with the judicious use of other drugs such as ephedrine and guanidine. Myasthenia at present is not known to vary with the level of the blood sugar or with the ingestion of food.

NOTES AND COMMENTS

Electric Shocks from Car Handles.—Dr. AGNES S. NUTT (Sheffield) writes: Shortly after the delivery of a new car, during a rather dry period I became aware of receiving shocks on leaving the car if I closed the door or touched the running-board. The makers suggested that the introduction of an eggcupful of water into the inner tubes of the tyres would stop the phenomenon—this would seem to act in the same way as the trailing chain, or the metal-containing tyre used in public service vehicles. It should be done at a service station, since it involves deflating the tube and removing the valve in order to introduce the water. The remedy has so far been effective.

Dr. J. E. KING (Blackpool) writes: Dr. W. W. Fulton (July 14, p. 132) suggests that no person will receive a shock other than the driver or other occupant of the car. This is certainly not true, as the policeman who pulled me up the other day found to his annoyance when he opened the car door. Incidentally, I often experience this static shock, but I never wear rubber-soled shoes.

Auriculo-temporal Syndrome.—Mr. H. A. HAXTON (Manchester) writes: In "Any Questions?" (July 21, p. 190) there is a note on the auriculo-temporal syndrome which does not take into consideration the more recent observations on this subject. In my paper (*Brain*, 1948, **71**, 16) I reported a case in which the typical auriculo-temporal syndrome could be temporarily abolished by procaine injection of the stellate ganglion. The gustatory sweating which sometimes follows operations on the cervico-thoracic portion of the sympathetic chain responds similarly. These findings evoked the theory that the syndrome is due to the action of acetylcholine, liberated at intact sympathetic nerve endings, on adjacent sweat glands and vessels which have become sensitized because of damage to their sympathetic nerve supply. The older theories do not fit the findings and must be discarded. As regards treatment, any case of auriculo-temporal syndrome in which the symptoms are sufficiently distressing should be investigated by procaine block of the stellate ganglion, and if the condition is thereby temporarily relieved the logical treatment is stellate ganglionectomy.

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